American Journal of Diseases of Children

VOLUME 31 APRIL, 1926 NUMBER 4

BILIARY CIRRHOSIS

REPORT OF A CASE WITH ATRESIA OF THE INTRAHEPATIC BUT WITHOUT ATRESIA OF THE EXTRAHEPATIC BILE DUCTS, AND WITH A STUDY OF ITS METABOLISM *

LEONARD G. PARSONS, M.D., F.R.C.P. (LONDON)

AND

EVELYN M. HICKMANS, PH.D., M.SC. (BIRMINGHAM)

BIRMINGHAM, ENGLAND

This case, which forms the basis of this paper, came under the observation of one of us during an investigation, by balance experiments, of the metabolism of atrophic infants. During life, the condition was diagnosed as one of congenital obliteration of the bile ducts, and it was thought that a study of the absorption and retention might prove useful in observing the effect of a low fat absorption on the absorption of calcium, phosphorus, carbohydrate and protein.

The importance of disorders of fat digestion in producing infantile atrophy has been largely stressed by the German school, particularly by Czerny and Finkelstein. The former believes that the cause of atrophy is demineralization of the body, the demineralization being the result of inability to assimilate fat, and the formation of fatty acids in excess. To neutralize these acids, alkalis are taken from the tissues; in constipation, calcium; in diarrhea, sodium and potassium are thus excreted. Finkelstein holds that in atrophy the normal relationship between fat and carbohydrate is disturbed. Both authorities postulate that in atrophy there is diminished absorption of fat. These views have received wide support and are still held by many pediatricians. Of recent investigations into fat absorption those of Utheim [1] and Hutchison [2] yielded some support to this theory, but in a large number of observations carried out by us, using rigid precautions, we were unable to confirm these observations.[3] We found that although fat absorption in artificially fed wasting babies varied to some degree with the type of

* Received for publication, Jan. 8, 1926.

* From the Children's Hospital, Birmingham.

1. Utheim, K.: J. Metabol. Res. **1**:801, 1922.
2. Hutchison, H. S.: Quart. J. Med. **13**:277 (April) 1920.
3. Parsons, L. G.: Goulstonian Lectures on some Wasting Diseases of Early Infancy, Lancet **1**:687 (April-May) 1924.

food given, yet atrophic children were able to absorb and digest fat as well as normal children, if they were not suffering from diarrhea at the time of the experiment. Fleming and Hutchison,[4] examining a smaller number of children, came to the same conclusion. We have now carried out observations on 100 atrophic infants, and the results previously reported have been confirmed. The opportunity of examining a case in which large amounts of fat are unabsorbed because of some organic disease was therefore welcomed.

REPORT OF CASE

N. C., a girl, was 2 months old when admitted into hospital on May 4, 1925. She was the sixth child; the other children were all alive and healthy. She was a full term child, breast fed for fourteen days only, and then fed on a milk mixture. The child was normal for the first three weeks of her life; she then developed jaundice, the urine became dark, and the stools clay colored. There were no other symptoms, except that she had been losing weight for some time prior to her admission to hospital.

On admission, the child was jaundiced, weighed 8 pounds, 10 ounces (3.9 Kg.), and appeared quite well nourished. The liver was enlarged, reaching almost to the umbilicus, and was very firm to the touch. The spleen was not palpated. There were purpuric patches on the buttocks and thighs. The stools were clay colored, and the urine showed a large amount of bile. The Wassermann reaction was negative.

Progress.—The jaundice varied slightly in degree, sometimes a little less, sometimes a little more pronounced than on admission. In the fortnight or so immediately preceding the child's death, the color had become rather less marked, and the stools showed a slightly slate tint. During the rest of the time they were clay colored. The urine was always bile stained. The child's weight at death was 7 pounds 6 ounces, the loss of weight (1 pound 4 ounces) during the time she was in hospital being very gradual; indeed, on two or three occasions there was an actual gain in weight. Vomiting occurred once only, and that was following an attempt to feed the child on a high fat diet. The baby died suddenly on August 24, sixteen weeks after admission into hospital.

Necropsy.—The organs were bile stained. The peritoneum contained many large, dark glands, and similar glands were present at the hilum of the liver. The liver weighed 365 Gm., was large and dark green, its surface was finely granular, and it was obviously very cirrhotic. The gallbladder was approximately of normal size, and did not show any changes suggesting atrophy or previous inflammation; it contained bile, and pressure on it resulted in bile passing along the cystic and common bile ducts, entering the duodenum through the papilla. There was no obstruction found in the cystic duct nor in the bile ducts between their exit from the liver and entrance into the duodenum. Dissection also failed to reveal any obstruction from external compression, and the glands before described did not press on the ducts. The spleen weighed 50 Gm., was large, but not unduly firm, and was dark red. There was nothing abnormal in the other organs except bile staining. There was no evidence of rickets nor of syphilis.

Microscopic sections of the liver showed an advanced "biliary cirrhosis," many of the smaller bile ducts being plugged and distended with inspissated bile, the picture being exactly similar to that seen in congenital obliteration of the bile ducts. In sections taken near the hilum of the liver, some of the

4. Fleming, G. B., and Hutchison, H. S.: A Study of Metabolism in the Undernourished Infant, Quart. J. Med. **68**:339 (July) 1924.

large bile ducts were patent and not distended, whereas others in close proximity appeared distended, and contained inspissated bile. The smaller bile ducts were so distended and plugged with bile that we are forced to the conclusion that there must have been some obstruction to the bile ducts, before they emerged from the liver. The presence of bile in the gallbladder, and the microscopic appearance of the liver near the hilum, showed that this obstruction was either intermittent, or did not involve all the bile ducts. There was no evidence of cholangeitis, and sections stained by Levaditi's method failed to reveal the presence of spirochetes. Sections of the pancreas showed a moderate degree of fibrosis.

During the child's lifetime, although slight variation in the depth of the jaundice was noticed at times, no doubt was entertained but that the condition was one of congenital obliteration of the bile ducts. The obstruction to the bile flow must, however, have been almost complete, because of the condition of the liver, and the symptoms presented by the child, that is, intense icterus, pale stools and biliuria. However, in view of the necropsy findings, the specimens of dried feces were examined for the presence of bile pigments and bile salts, by Schmitt's corrosive sublimate test and by Pettenkoffer's test, respectively. In none of the specimens was the test for bile pigments positive, but a slight reaction for bile salts was obtained in all the stools. It is now generally held that bile salts are formed by the hepatic parenchyma, but that bile pigments may be formed elsewhere: indeed the presence of stercobilin has been demonstrated in the rectum after ligature of the common bile duct. The absence of bile salts in the feces may, therefore, be taken as conclusive evidence of exclusion of the bile from the intestine. It is obvious therefore that only traces of bile were finding their way into the duodenum. Confirmatory evidence of this statement is also found in the fact that the cholesterol content of the feces in each case was much lower than the normal.

Two well known theories have been advanced to explain the association of hepatic cirrhosis with congenital obliteration of the bile ducts. In John Thomson's view, there is, in the first place, a developmental aplasia, or narrowing of the bile ducts, which gives rise by obstruction to cirrhosis. Sir Humphrey Rolleston, on the other hand, believes that as a result of a placental toxemia there is, first, a mixed cirrhosis of the liver which gives rise to a descending obliterative cholangeitis.

We have examined the sections of the liver from our subject very carefully for evidence of cholangeitis, but without success; the cirrhosis was biliary and was not a mixed form. At the same time, we feel that this case lends little support to the view that the cirrhosis follows on a developmental defect of the bile ducts, but suggests that whatever be the cause of the condition it is one which attacks the liver parenchyma at as early a stage as the bile ducts, and offers definite evidence that the whole process may be an intrahepatic one. If this view is correct, surgical intervention, at any time after the diagnosis is made, cannot offer any chance of complete recovery, because a marked cirrhosis of the liver must be present. In this patient, surgical treatment would obviously have been quite useless.

METABOLISM STUDIES

In order to determine whether large quantities of fat in the intestine adversely affected the absorption of other elements in the food, Fleming [5] studied the respiratory exchange in a case of biliary atresia, and came to the conclusion that large quantities of fat delayed the absorption of carbohydrate to a moderate degree. On the other hand, Muriel

5. Fleming, G. B.: The Respiratory Exchange in a Case of Biliary Atresia, Am. J. Dis. Child **23**:66 (Jan.) 1922.

Brown [6] showed that blood sugar curves, in normal and in marasmic babies, were not altered by increasing the amount of fat in the food, from which she concluded that a high fat content in the diet did not interfere with the rate of absorption of carbohydrate. However, this worker is careful to point out that in making such a deduction it is necessary to assume that the blood sugar content is really a gage of the absorption of carbohydrate, and to remember that hepatic and pancreatic efficiency will also modify the amount of carbohydrate circulation in the blood.

In our case, absorption and retention figures were determined for fat, protein, calcium and phosphorus. These were obtained during three periods on a dietary of cow's milk, water and dextrimaltose, the amount

TABLE 1.—*Intake in Grams of Fat, Carbohydrate, Nitrogen, Calcium and Phosphorus Per Twenty-Four Hours*

	Diet 1	Diet 2	Diet 3
Fat	12.93	22.90	18.36
Carbohydrate	19.24	20.86	70.36
Nitrogen	2.82	3.25	3.38
Calcium (as CaO)	0.98	1.44	0.92
Total phosphorus (as P_2O_5)	1.069	1.316	1.431
Inorganic phosphorus (as P_2O_5)	0.665	0.888	0.99

TABLE 2.—*Fat Metabolism* *

	Diet 1	Diet 2	Diet 3
Fat intake in grams	12.93	22.90	18.36
Fat output in grams	8.96	12.28	13.24
Percentage absorption	30.7	46.1	27.9
Weight of dried feces in grams	12.4	15.6	22.0
Percentage of fat in dried feces	72.2	78.6	60.2
Distribution of fecal fat (percentage of total fat)			
Saponified	40.2	51.4	52.9
Free fatty acid	37.3	28.9	25.8
Neutral fat	22.6	19.8	21.3

* These figures are for twenty-four hour periods.

of fat in the diet being different in each period. The amount of carbohydrate during the first two periods was almost identical, but during the third period, additional carbohydrate was given. The intake per day in grams of fat, carbohydrate, nitrogen, calcium and phosphorus on each of these dietaries is shown in table 1.

Each diet was continued for a period of eight days, and during the last five days of this time, the child was placed on a metabolism bed. The full details of this method have been previously described by us. The results obtained are shown in tabular form (tables 2 to 5), the

6. Brown, M. J.: The Sugar Content of the Blood in Normal and Undernourished Children, and the Effect of Fat on the Absorption of Carbohydrate, Quart. J. Med. **70**:175 (Jan.) 1925.

figures given are for twenty-four hour periods, and are the averages of the five days' estimates.

The stools were abnormally large, and contained a large percentage of fat. The correctness of this observation is best demonstrated by comparing the weight of the stools and the percentage of fat contained in them, with the corresponding results obtained from wasted infants. In eighty-two cases of infantile atrophy, the daily average weight of dried feces was 6.0 Gm. and the average percentage of fat in the stool 36.8 Gm. While it is true that the percentage of fat in the dried feces from cases of atrophy has varied within wide limits (from 11.5 to 63.5) yet, as a general rule, we have found that when the stool was a bulky one it contained a high percentage of fat.

Fat splitting on the whole was efficient, although the amount of unsplit fat was distinctly greater than we have found in wasted infants; in the latter the average figure for neutral fat has been 8.3 per cent of

TABLE 3.—*Nitrogen Metabolism* *

	Diet 1	Diet 2	Diet 3
Intake in grams	2.824	3.250	3.382
Output in feces in grams	0.327	0.276	0.389
Output in urine in grams	1.702	2.420	2.266
Amount absorbed in grams	2.49	2.97	2.993
Amount retained in grams	0.82	0.55	0.727
Percentage absorption	88.4	91.5	88.5
Percentage retention	28.9	17.0	21.5

* These figures are for twenty-four hour periods.

the total fat. The amount of fatty acid is also larger than the average for wasted infants, which was 20.1 per cent of the total fat.

From the table it will be seen that the absorption is quite poor, and this again may be compared with the average absorption in artificially fed atrophic children, which shows a figure of almost 88 per cent. The amount of fat absorbed, and the percentage of absorption varied on the different dietaries, were actually highest on the one containing the largest amount of fat.

Our results may be compared with those of Koplik and Crohn.[7] These authors investigated the fat and nitrogen metabolism in a patient, in whom the condition was clinically one of congenital obliteration of the bile ducts, but on whom a necropsy was not performed. Observations were made over four-day periods, but the daily intake varied considerably, and there was no preliminary period of constant dietary before the child was placed on the metabolism bed. They found that

7. Koplik, H., and Crohn, B. B.: Fat and Nitrogen Metabolism in a Case of Congenital Absence of the Bile Ducts, with a Study of Ferments of the Pancreatic Secretion and the Feces, Am. J. Dis. Child. **5**:36 (Jan.) 1913.

fat splitting was poor, and that 48.4 per cent of the fat was absorbed. They quote a case of Neimann's in which the fat absorption varied from 28 to 39 per cent, but do not say whether fat splitting was normal. On the other hand, Telfer [8] has investigated the fat splitting in a similar case; his results show even better fat splitting than in our case, and the presence of a large amount of fatty acid in the stool.

The nitrogen absorption on all these dietaries is almost identical, and is very good, but the retention is not so satisfactory, and it may be noted that the lowest retention is obtained in the highest fat dietary. Koplik and Crohn [7] found a nitrogen absorption of 86.2 per cent and a retention of 32.6 per cent; and Neimann [9] found an absorption of 80 to 93 per cent. The average figures we have obtained in wasted infants have been absorption, 86.8, and retention, 49.6 per cent, which if compared with the values obtained in the present case, show that the presence of large quantities of unabsorbed fat in the intestine does not adversely affect nitrogen metabolism.

TABLE 4.—*Calcium Metabolism* *

	Diet 1	Diet 2	Diet 3
Intake in grams	0.98	1.44	0.92
Output in feces in grams	1.05	1.50	1.11
Output in urine in grams	0.05	0.06	0.07
Amount absorbed in grams	[—0.07]	[—0.06]	[—0.19]
Amount retained in grams	[—0.12]	[—0.12]	[—0.27]
Per cent absorption	Negative	Negative	Negative
Per cent retention	Negative	Negative	Negative

* These figures are for twenty-four hour periods, and are expressed as calcium monoxid.

These results obtained from the observations on calcium metabolism furnish, perhaps, the most striking feature of this case since with each form of dietary there is a negative calcium balance. It has recently been shown (Hickmans [10]) that to insure a good absorption of calcium in atrophic children fed on milk and water mixtures, the fat intake should not be less than 12 to 14 Gm. daily, and that the best absorption of calcium takes place when there is a definite relationship between the calcium and fat intake, namely, when there is from 0.04 to 0.078 Gm. of calcium oxid for 1 Gm. of fat. These observations, however, were carried out on children whose fat absorption (with one exception) was not abnormal. According to these figures, the calcium and fat intakes were sufficient in the present instance, but from the point of view of absorption of fat, the case can only rightly be compared with a child fed

8. Telfer, S. V.: The Influence of Free Fatty Acids in the Intestinal Contents on the Excretion of Calcium and Phosphorus, Biochem. J. **15**:347, 1921.
9. Neimann, quoted by Koplik and Crohn: Ztschr. f. Kinderh. **4**:152, 1912.
10. Hickmans, E. M.: The Calcium Metabolism of Atrophic Infants, and Its Relationship to Their Fat Metabolism, Biochem. J. **13**:925, 1924.

for prolonged periods on a low fat dietary, under which conditions we know that a negative calcium balance may occur.

Calcium was estimated in the urine as well as in the feces. The fecal output alone, however, was actually higher than the intake, a state of affairs which can only be explained by the endogenous origin of at least some of the calcium of the feces. The results obtained further emphasize the necessity for a good fat absorption to insure an adequate absorption of calcium, since a poor fat absorption probably means an inadequate absorption of the fat soluble vitamins (the growth vitamin and calcium depositing vitamin). In this connection it is of interest to note that at the necropsy on this child, there was no evidence of rickets. The question of calcium absorption will be referred to again, in connection with phosphorus metabolism. The proportion of calcium passed in feces as soap was 34.3, 42.0 and 63.0 per cent on the three dietaries. These figures are higher than normal, thus Telfer [11] states that in normal children from 20 to 30 per cent of the calcium of the feces is passed

TABLE 5.—*Phosphorus Metabolism* *

	Diet 1	Diet 2	Diet 3
Intake in grams	1.069	1.316	1.431
Output in feces in grams	0.085	0.188	0.156
Output in urine in grams	0.428	0.735	0.717
Amount absorbed in grams	0.984	1.128	1.275
Amount retained in grams	0.556	0.393	0.558
Per cent absorption	92.1	85.7	97.8
Per cent retention	52.0	29.9	39.1
Per cent of total output excreted in urine	83.5	79.6	82.1

* These figures are for total phosphorus (expressed as P_2O_5) and for a period of twenty-four hours.

as soap, and our figures, recently published for marasmic children showed 28 per cent of fecal calcium passed as soap on cow's milk and water dietaries, 13 per cent on skimmed milk, and 54 per cent on high fat dried humanized foods.[10]

On each dietary, the phosphorus absorption was excellent, but the striking feature is that by far the greater part (from 79.6 to 83.5 per cent instead of the normal 40 per cent) of the phosphorus excretion, was excreted by the kidneys (Telfer [11]). It may further be noted that on the second and third dietaries, in which the amount of fat excreted was practically the same, 12.28 and 13.24 Gm. respectively, the amount of phosphorus excreted in the urine was almost identical, being 0.735 and 0.717 Gm. Observations were made on the inorganic phosphorus metabolism, and these also showed the same marked increased excretion of phosphorus by the urine.

11. Telfer, S. V.: Studies in Phosphorus and Calcium Metabolism. Part I. The Excretion of Calcium and Phosphorus, Quart. J. Med. **61**:45 (Oct.) 1922.

Now, the relation of calcium to phosphorus metabolism has been the subject of considerable study. Orr and his co-workers [12] showed that excessive amounts of calcium in the diet tend to increase the total absorption and retention of calcium but to impair phosphorus retention, whereas excessive amounts of phosphorus in the diet influenced calcium metabolism unfavorably, and are accompanied by an increase of calcium in the feces. They point out that the retention of one element in the intestine by the presence of an excessive amount of the other, is best explained by the formation of insoluble phosphate of calcium. Telfer had previously come to similar conclusions. All these workers showed that on a high calcium dietary, considerable amounts of phosphorus are diverted from the urine to the stools, whereas with high phosphorus dietary, calcium excretion in the urine becomes less.

Telfer [8] has shown that with the persistence of an excess of fatty acid, such as occurs with the exclusion of bile from the intestine, less phosphorus is excreted by the feces, more by the urine, and that the deviation of phosphorus to the urine is roughly proportional to the amount of fatty acid in the feces. The following explanation of this deviation has been suggested by this author:

> The amount of phosphorus in cow's milk is in excess of the equivalent amount required to combine with all the calcium to form tricalcium phosphate. Calcium phosphate is soluble in the lower fatty acids, and it can be shown by experiments in vitro that precipitated calcium phosphate is redissolved in an excess of the volatile water soluble fatty acids of butter fat. The latter consist almost entirely of butyric and caproic acids. If the free fatty acids of fat hydrolysis persisted in excess in the intestine . . . the calcium phosphate, if initially precipitated, would tend to pass into solution. In the presence of the higher fatty acids and their soluble salts, a secondary reaction may then result, in the formation of insoluble calcium soaps, and the liberation of phosphoric acid. The calcium salts of the lower fatty acids are soluble and may be absorbed. . . . The phosphoric acid which has been liberated . . . may then be absorbed as it exists in soluble form.

Orr and his co-workers state that increased acidity of the intestinal tract results in the production of the more soluble primary phosphate from the insoluble secondary and tertiary forms, and should thus promote the absorption both of calcium and phosphorus. Telfer [13] has produced evidence showing that the absorption of calcium only takes place in the upper part of the intestinal tract. The solution of the calcium salts in the food is affected by the acid of the gastric juice, and

---

12. Orr, W. J.; Holt, L. E.; Wilkins, L., and Boon, F. H.: The Relation of Calcium and Phosphorus in the Diet to the Absorption of These Elements from the Intestine, Am. J. Dis. Child. **28**:574 (Nov.) 1924.

13. Telfer, S. V.: Studies in Calcium and Phosphorus Metabolism. Part III. The Absorption of Calcium and Phosphorus and Their Fixation in the Skeleton, Quart. J. Med. **67**:245 (April) 1924.

absorption proceeds until the acid mixture of lime and phosphoric acid is rendered alkaline by the intestinal secretions, when calcium phosphate is precipitated in insoluble form. It would, therefore, appear correct that an increased acidity in the upper part of the intestinal tract should increase the absorption of calcium, and, as a matter of fact, in two out of three wasted infants fed on acidified milk (having an approximate p_H 5.2 to 6.0) we found that the calcium absorption was considerably above the average.

Bogert and Kirkpatrick [14] have also shown that foods which are acid forming improve the absorption of calcium. The fact that in the case described in this paper there is a persistent negative calcium balance, in spite of an excess of free fatty acid in the intestine, suggests that there is some other factor concerned in calcium absorption; also that when large amounts of fat are unabsorbed, calcium absorption will be poor, even should the intestinal contents be more acid than normal, from the presence of an excess of free fatty acid. It is quite possible that the other factor is the fat soluble antirachitic vitamin.

The suggestion, that increased acidity promotes the absorption of phosphorus, is supported by the results obtained by Telfer in his case of biliary atresia, and by our results. We have also recently investigated the phosphorus metabolism of two wasted infants, fed on lactified milk, and in both instances there was a deviation of the excreted phosphorus from the feces to the urine, exactly similar to that occurring when bile is excluded from the intestine. These are the only instances known to us in which the effect of acid diets on phosphorus metabolism has been observed in infants, although the converse has been shown by Orr, who found that both calcium and phosphorus absorption are unfavorably influenced by diets that increase the alkalinity of the stools.[15]

SUMMARY

1. A case of biliary cirrhosis is described, in which there is evidence of obstruction of the bile ducts, but not in their extrahepatic course.

2. The argument is brought forward that this case supports the view that the hepatic cirrhosis occurs in at least as early a stage of the disease as the changes in the bile ducts.

---

14. Bogert and Kirkpatrick: Studies in Inorganic Metabolism, II. The Effects of Acid Forming and Base Forming Diets on Calcium Metabolism, J. Biol. Chem. **54**:315 (Oct.) 1922.

15. The methods used in this investigation were as follows: Cholesterol was estimated by Gamble and Blackfan's method; nitrogen by Kjeldahl's method; calcium by McCrudden's method; fat by Hickmans' modification of the Rose-Gottlieb method and phosphorus by the method described by Bell and Doisy.

3. Metabolism balance experments show that:

A, fat is well split; there is an increased formation of fatty acid; fat absorption is poor.

B, nitrogenous absorption is good.

C, there is a negative balance for calcium.

D, phosphorus absorption is good; a very great proportion of the excretions of phosphorus is via the urine.

4. The presence of large quantities of unabsorbed fat in the intestine—due to the exclusion of bile—resulted in a negative calcium balance, and a deviation of phosphorus to the urine, but had no effect on the absorption of nitrogen.

CHRONIC INTERSTITIAL HEPATITIS

WITH REPORT OF A CASE *

GEORGE F. MUNNS, M.D.
CHICAGO

This case is reported because of the apparent rarity of the condition. Cirrhosis of the liver occurring in infants, secondary to congenital syphilis or atresia of the bile ducts, is relatively common and many such cases have been reported, but neither of these conditions was present in the case reported here.

REPORT OF CASE

The patient, a boy, aged 11 months, was admitted to the pediatric service of the Presbyterian Hospital on March 18, 1925, with the complaint of jaundice, constipation, and failure to gain weight.

Past History.—The patient was born April 10, 1924, at the Iowa State University Hospital. He was the first baby; the birth was spontaneous and delivery was normal, and the infant appeared normal. Wassermann reactions of the blood of both mother and child were negative at this time.

Circumcision was performed on the tenth day. The wound began to bleed that night and continued to bleed for three days, when bleeding also began from the umbilicus. The hemorrhage was finally controlled on the fourteenth day by a transfusion of the mother's blood (10 cc. intramuscularly had failed to control the hemorrhage previously). On the eighteenth day jaundice was noticed for the first time; the stools were still yellow, but on the twentieth day they became clay colored.

May 12, 1924, the infant was admitted to the Pediatric Service of the State University of Iowa Hospital, at the age of 32 days. At this time the blood count was normal and the urine was negative. Jaundice continued with varying degree of intensity. The stools were light colored except when bile was given by mouth. On the sixteenth day in hospital, there was an elevation of temperature, accompanied by diarrhea, which cleared up promptly. The blood Wassermann was again negative. The Pirquet test and the urinalysis gave a negative bile reaction. The infant gained weight steadily and the general condition seemed fairly good. Variations in the intensity of the icterus, together with occasional elevations of temperature continued. On August 24, the patient was adopted and was removed immediately from the hospital by the foster parents.

Examination at time of admission to the Presbyterian Hospital revealed a small, jaundiced, poorly nourished white male infant, apparently not acutely ill. The only significant physical findings at this time were: generalized marked icterus, linear scratch marks on the abdomen, moderate generalized adenopathy, slight beading of the ribs and enlargement of the epiphyses of the long bones. The liver was 4 cm. below the costal margin; the spleen was palpable and enlarged.

At the time of admission the stools were acholic, the Wassermann reaction of the blood and the Pirquet test were negative; urinalysis was negative except for a trace of bile. The blood hemoglobin was 80 per cent; red blood cells, 4,520,000; white blood cells, 22,650; polymorphonuclears, 42 per cent; small mononuclears, 52; large mononuclears, 4; transitionals, 2. The van den Bergh blood reaction was indirect; the fragility blood test (Griffin-Sanford technic) was read at the end of one hour. Hemolysis began at 0.42 per cent sodium chloride solution; it was

* Received for publication, Feb. 16, 1926.

complete at 0.28 per cent. Roentgenograms of the long bones revealed only moderate rachitic changes. On the second day after admission, the temperature rose to 102 F., with no physical findings to account for the rise except a rather mild nasopharyngitis. The temperature was normal the following day. On the fourth, sixth, seventh and eighth days after admission, the temperature rose to 100 F. each day, usually in the afternoon.

The patient was put on a diet of albumin milk feedings. His appetite was quite variable; there was a distinct tendency toward constipation together with several rather severe attacks of distention, which were usually relieved promptly by an enema and a rectal tube. The stools continued to be acholic for the most part, but occasionally were yellow. The general condition seemed improved, and on the twenty-fifth day he was discharged, still quite jaundiced, but having made a gain of 18 ounces in weight. The diagnosis at this time was congenital atresia of the bile ducts.

On June 8, 1925, fifty-seven days after discharge, the patient was readmitted to hospital. The mother complained at this time that the jaundice had increased and that the child had failed to gain weight for one week previous to admission. She said that up to this time he had been doing fairly well, was taking cereal, vegetables and whole milk, gaining weight, had cut two lower central incisors and had been passing from three to four soft yellow stools daily. The jaundice had increased, however, and the urine had begun to stain the clothes.

Examination at this time revealed an undernourished, markedly jaundiced, white male infant, age 14 months. He could sit up alone but could not stand; he had only two teeth and he was distinctly rachitic. The abdomen was distended and the liver was greatly enlarged, the lower edge being half-way between the lower rib margin and the umbilicus. The spleen was also greatly enlarged.

Blood hemoglobin, 50 per cent; red blood cells, 3,020,000; white blood cells, 26,000.

Fragility Test: Hemolysis began at 0.38 per cent sodium chloride solution and was complete at 0.28 per cent. Bleeding time, twelve minutes; coagulation time, three minutes. The urine showed a trace of albumin. The bile test was positive.

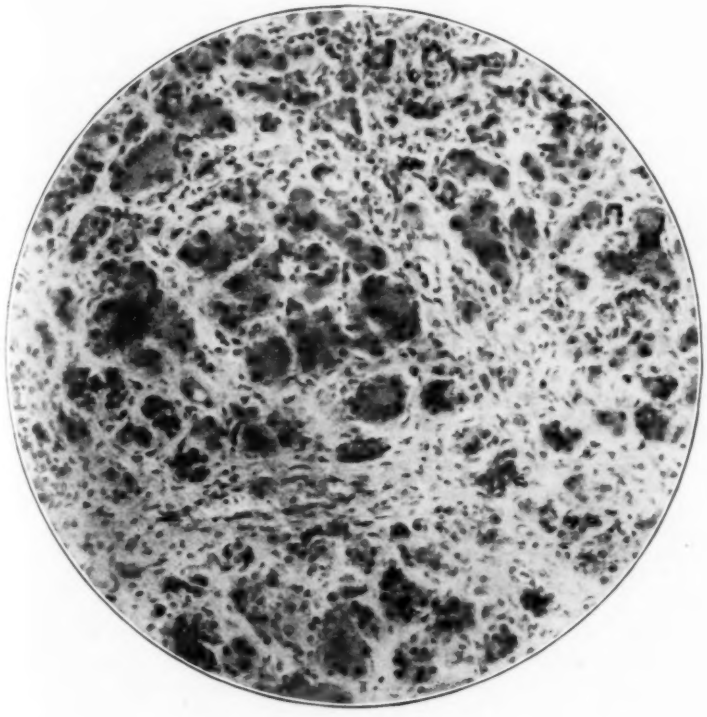
The patient stayed in the hospital for six days, and during this time had daily elevation of temperature never higher than 100.8 F., usually ranging from 99.8 to 100 F. This elevation of temperature always occurred in the afternoon.

An operation was advised at this time, but permission was refused and the patient was taken home by the parents. Twenty-eight days later, the child was again admitted to the hospital. At this time the mother said that the child's abdomen had been greatly enlarged for about one week, that the jaundice had increased and the child had become drowsy. She had not noticed the color of the stools, but said there had been from two to three daily, which she believed were yellow.

Examination revealed a markedly jaundiced, undernourished, drowsy child, with great enlargement and distention of the abdomen, together with edema of the face and extremities. The mucous membranes were pale and yellow. The lungs were clear, but the heart was enlarged to the left and there was a loud systolic murmur heard best at the apex. The abdomen was tense and shiny, with shifting dulness and bulging in the flanks. The liver and spleen could not be palpated owing to the distention. An abdominal paracentesis was immediately performed, and 450 cc. of thin, clear, straw colored fluid was removed. Cultures were made and were reported negative for any organisms. Following the removal of the fluid, the liver and spleen could be palpated easily and were both greatly enlarged. The liver felt quite hard. The blood at this time revealed the following picture: hemoglobin, 60 per cent; red blood cells, 3,120,000; white blood cells, 35,000; polymorphonuclears, 39 per cent; small mononuclears, 59 per cent; large mononuclears, 1 per cent; transitionals, 1 per cent. The van den Bergh test had a direct reaction on the blood and ascitic fluid. The urine was dark, gave a strongly positive bile test; albumin was positive; there were no casts, red blood cells or

white blood cells. The stools were yellow to brown, one to three daily. The following day 250 cc. of fluid was removed from the abdomen. The edema of the face and extremities increased meanwhile. The appetite was poor, the child was quite drowsy and the temperature ranged between 100 to 101 F. Fluid again accumulated in the abdomen rapidly, and the general course was steadily downhill.

On July 18, 610 cc. of fluid was removed from the abdomen. On the following day the general condition was poor. The temperature was 102 F., respiration 60, pulse 136, and the next day scattered fine râles could be heard over both lung fields. The blood picture at this time was hemoglobin, 35 per cent; red blood cells, 2,800,000; white blood cells, 48,000; polymorphonuclears, 53 per cent; small mononuclears, 41 per cent; transitionals, 3 per cent; eosinophils, 3 per cent.



Section of liver.

The temperature rose gradually to 103.8 F., the heart tones became progressively weaker, râles in the lungs increased and death occurred on July 21, about fourteen months after the appearance of the first symptom.

Necropsy findings were reported by Dr. Carl W. Apfelbach.

Gross and Microscopic Alterations.—The body was that of a white, male, child, aged about 15 months, weighing 11 pounds, and about 76 cm. in length. The skin of the entire body was pigmented light yellow. The abdomen was protuberant, the extremities and neck were thin, and the skin was loose.

In the peritoneal cavity, there was about 500 cc. of light yellow-brown, clear, watery fluid. The lower margin of the left lobe of the liver was two fingers' breadth above the lower costal margin. The spleen, appendix vermiformis and sigmoid portion of the colon were normally free. The mesentery of the small bowel and most of the retroperitoneal tissues were infiltrated with light yellow watery fluid. The peritoneum generally was pale gray-brown and translucent.

The loops of the small bowel were from 2 to 2.5 cm. in diameter; the lower loops were filled with gas and a moderate amount of pale yellow-brown, soft material. In the duodenum and jejunum the intestinal content was light yellow. The gallbladder was firmly adherent to the mesocolon and colon by firm fibrous adhesions.

The ampulla of Vater, and the common, hepatic and cystic ducts were patent. At its middle the common bile duct averaged from 3 to 4 mm. in circumference, and 1 cm. from the ampulla it was 6 mm. The right hepatic duct was uniformly 4 mm. in circumference, the left was from 2 to 3 mm. The lining of these ducts was smooth, thin and stained yellow. The wall of all of the extrahepatic biliary tract was thin. In the gallbladder, there was about 5 cc. of light yellow mucus; the lining was normally thin.

The liver was firm in consistency; it was 13.7 cm. wide. The right lobe was 7.6 cm. long and 3.7 cm. thick; the left was 7.5 cm. long and 2 cm. thick. The capsule was thin and transparent, and the surface was smooth. Throughout, this organ was dark olive green; surfaces made by sectioning were mottled dark and light olive green. The dark places were irregular, from pin point to 2 mm. in diameter, and separated by the light olive green regions which form a network throughout the surfaces. The mottling was quite uniform throughout both lobes.

The spleen was slightly enlarged, the capsule was thin and surfaces made by sectioning were light purple and flat. The malpighian corpuscles were numerous, averaging 1 mm. in diameter, and occupied about one third of the surfaces made by sectioning.

There was no gross noteworthy change of the lining of the portal vein and its large tributaries, of the hepatic artery, stomach, small and large bowel, urinary bladder, rectum, or of the pancreas and prostate. Only the abdominal organs were examined.

Addendum.—In microscopic preparations of the liver fixed in Zenker's fluid and embedded in paraffin, stained with hematoxylin and eosin, the normal lobular arrangement was entirely replaced by irregular groups of large and small epithelial cells and fibrous tissue. The large epithelial cells resembled hepatic cells in size and shape, were in irregular groups of ten to fifteen, and were separated by narrow and wide strands of old fibrous tissue, much of which was homogeneous and took the eosin stain. There was an abundance of brown pigment in the large epithelial cells. In other places in which the fibrous tissue was more cellular, the epithelial cells had a small amount of cytoplasm and were arranged in irregular, round to oval to long cords, composed of five to twenty cells. The nuclei of the small epithelial cells stain darker blue than those of the larger. Very few, if any, of the small epithelial cells contained brown pigment. The identification of the central veins and periportal tissue in most places could not be made. The interstitial tissue was composed almost entirely of old fibrous tissue with occasional small groups of cells resembling small lymphocytes. The heaviest bands of fibrous tissue were in most places about or near blood vessels. In addition to the brown pigment in most of the large epithelial cells, there was also similar green pigment in a few places.

Anatomic Diagnosis.—Extensive chronic interstitial hepatitis; marked generalized icterus; ascites; edema of the mesentery of the small bowel and retroperitoneal adipose tissue; hyperplasia of the spleen; marked emaciation; slight general anemia; paracentesis wound of the abdominal wall; fibrous adhesions between the gallbladder, the colon and the mesocolon.

COMMENT

The etiologic agent in the case could not be determined. Possibly, there was a slow infectious process as evidenced by exacerbations and remissions in the signs and symptoms, particularly the frequent and intermittent rises in temperature.

Gilford [1] believes that defective development must play a large part, and classifies such cases, although he refers to the condition in older children as instances of Hanot's splenomegalic form of hypertrophic cirrhosis.

J. H. Musser,[2] S. K. Mukherji,[3] Ghose [4] and others, report a large number of somewhat similar cases occurring among infants in India. The pathologic description tallies in many ways with the foregoing, but the youngest child in this series was 3 months old, and in the large majority the first symptoms occurred after 6 months. Errors in the diet are given as a possible cause for the relatively frequent occurrence of the condition in India.

There is only one closely similar case in the American literature, namely, that reported by C. H. Dunn.[5] Hatfield's [6] two cases, reported in 1889, are similar in only a few respects. Death occurred at the age of 2 weeks in both of these infants. Porter [7] reports one case which is similar to this in many respects.

SUMMARY

A case of chronic interstitial hepatitis occurring in an infant, the first sign of which appeared on the eighteenth day, is reported.

Since 1885, numerous cases of cirrhosis of the liver in older children have been reported. Some of these were explained on the basis of congenital syphilis, some by biliary obstruction, and others had no discoverable cause. Cirrhosis of the liver in infants and of the type described in our pathologic report is apparently a rare condition.

Excluding the cases reported from India, which resemble our case in many respects, we were able to find only two closely similar cases.

---

1. Gilford, H.: The Disorders of Post Natal Growth and Development, p. 265.
2. Musser, J. H.: Supplement to Cyclopedia of Children's Diseases, 1899, p. 798.
3. Mukherji, S. K.: Infantile Cirrhosis of Liver. Indian M. R. Book Dept., Calcutta, 1922.
4. Ghose: Lancet **1**:321, 1895.
5. Dunn, C. H.: Interstate M. J. **23**:14, 1916.
6. Hatfield, M. P.: Tr. Am. Ped. Soc. **1**, 1889.
7. Porter, L.: Abt's Pediatrics **3**:656, 1925.

DEATH FOLLOWING THE INHALATION OF ZINC STEARATE*

KARL SCHLAEPFER, M.D.
MILWAUKEE

REVIEW OF THE LITERATURE

This report deals with an instance of asphyxia and death following the accidental inhalation of zinc stearate. That untoward consequences follow inhalation of this powder, so universally used in the care of infants, appears to have escaped notice until 1922, when Heiman and Aschner [1] called attention to the fact. At that time Heiman reported

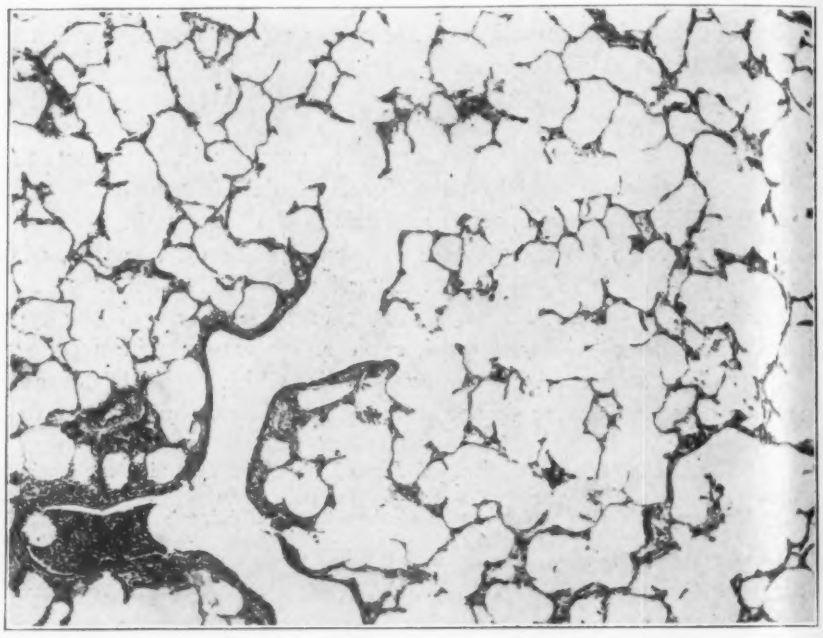


Fig. 1.—Photomicrograph showing the emphysema. In the lower part of the field, a small, distended bronchus is filled with an amorphous material and with leukocytes (×70).

his experience with twelve such instances. Rapid respiration and cyanosis were observed immediately after inhalation of the powder in eleven patients. Eight of these recovered within three days, while

* Received for publication, Nov. 10, 1925.

* From the Brady Laboratory of Pathology and Bacteriology, Yale University School of Medicine.

1. Heiman, H., and Aschner, P. W.: The Aspiration of Stearate of Zinc in Infancy, Am. J. Dis. Child. **23**:503 (June) 1922.

bronchopneumonia delayed recovery in the remaining. In the twelfth instance, a child, aged 8 months, asphyxia developed immediately and death occurred within twenty-four hours. Necropsy revealed small areas of pulmonary consolidation.

Heiman's report stimulated interest in this new danger, and undoubtedly played a rôle in the creation of a special committee of the American Medical Association [2] in 1923 for further investigation of the subject. The committee collected thirty-four additional cases, all of which had occurred since April 1919, and concerned infants between the ages of

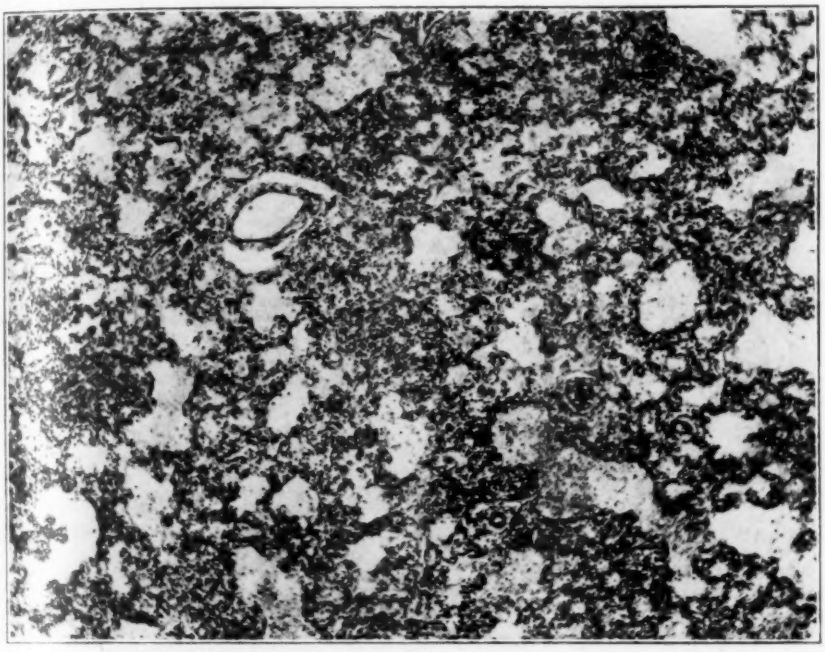


Fig. 2.—Photomicrograph taken from a partly atelectatic area with scattered areas of pneumonia. The alveoli are in part collapsed; in part they contain a homogeneous material, desquamated alveolar lining cells, red corpuscles and leukocytes. In some areas the alveolar epithelium has the appearance of a swollen, homogeneous band, devoid of nuclei (×70).

3 months and 2 years. In some, the powder was inhaled from the hand, into which it had previously been sifted from the can. In many, the container had been brought directly to the mouth of the child. One instance occurred when the lid of the container fell off; and still another when the powder was thrown into the face of the infant by an older child. In all thirty-four cases, symptoms were immediate following the inhalation of the powder. However, recovery took place in all but one

2. Special Article: Dangers of Zinc Stearate Dusting Powders, J. A. M. A. **83**:120 (July 12) 1924.

child, and, as a rule, was complete within two weeks, even when pneumonia had occurred. The one fatal instance was a child of 3 months, whose death resulted within an hour after inhalation of the powder.

A third fatality was reported by Edmonds [3] (1923). A child, aged 8 months, inhaled powder from the can with which he had been playing. Respiratory difficulty followed at once and became worse rather suddenly after a few hours. Death occurred in forty-eight hours.

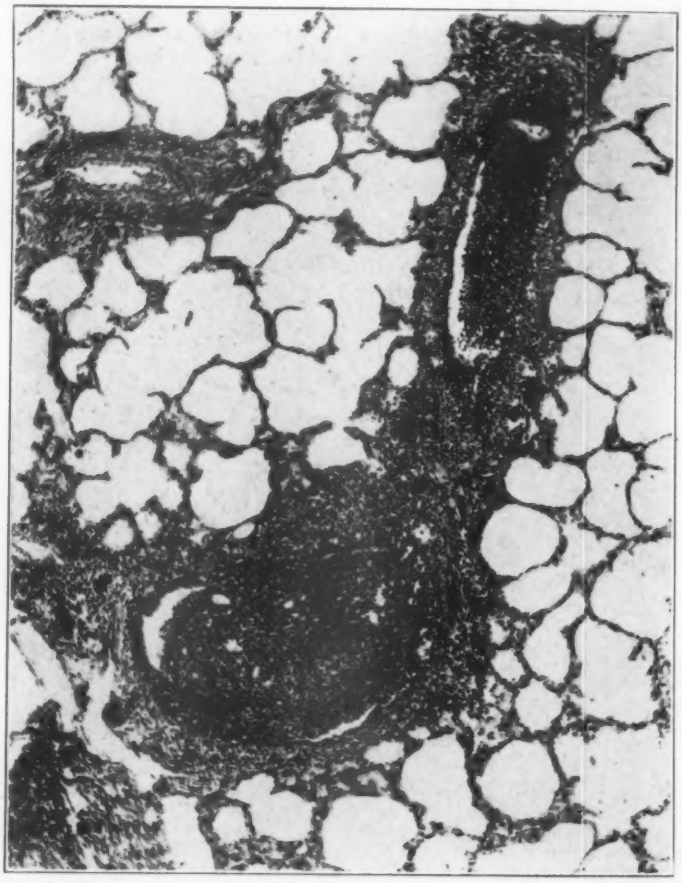


Fig. 3.—Bronchus filled with an amorphous material and with leukocytes (× 200).

Finally, O'Keefe [4] published a report of six instances with recovery, in children between the ages of 8 and 11 months.

The following report makes the fourth fatal instance in the literature.

3. Edmonds, W.: Pneumonia from Inhalation of Zinc Stearate Talcum Powder, J. A. M. A. **80**:105 (Jan. 13) 1923.

4. O'Keefe, Edward S.: Zinc Stearate Insufflation in Infancy, Boston M. & S. J. **191**:739 (Oct. 16) 1924.

CASE REPORT

C. H. H., a boy, aged 7½ months, was admitted to the New Haven Hospital, Nov. 28, 1923, in great respiratory distress following the inhalation of zinc stearate. The child had been well until the day before admission. Then, while the baby was lying on his back and playing with a box of stearate powder, the holes in the double rotating cover became patent and allowed a large amount of the stearate to be poured on his face. Screams attracted the family, who found the baby's face and mouth covered with powder. This was quickly wiped

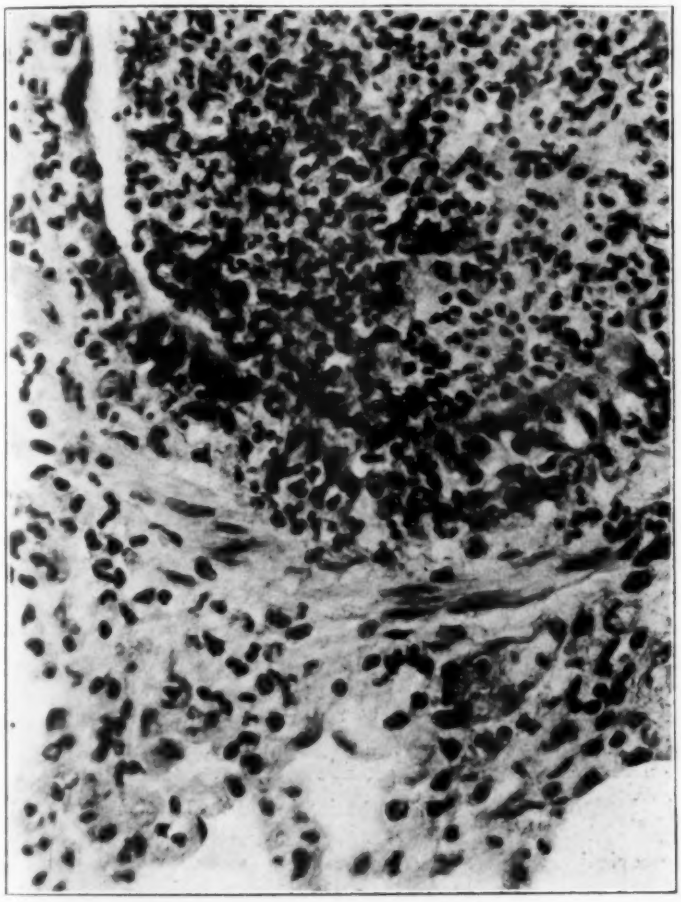


Fig. 4.—The bronchial epithelium is thicker and proliferated; the lumen of the bronchus is filled with an amorphous material and with leukocytes (× 350).

away, but the seriousness of the child's condition was noted immediately. Cyanosis was marked at once, and thereafter periods of deep cyanosis and labored respiration alternated with periods of pallor and exhaustion. Twenty-four hours after the accident the infant was brought to the hospital. Thorough physical examination was impossible. The child breathed with extreme difficulty. Retraction at the suprasternal notch and at the insertion of the diaphragm was visible. Oxygen inhalation and large quantities of saline solution intravenously seemed to cause slight temporary improvement. The child's temperature rose

from 37.8 C. (100 F.) on admission to 38.5 C. (101.2 F.) shortly before death. Necropsy was performed ten hours after death. The important findings follow.

The lungs were voluminous, almost touching each other at their anterior medial borders, and thereby covering the greater portion of the pericardium. The left lung weighed 65 gm., and the right 90 gm. Their general appearance was similar. Deep red areas of atelectasis, from 0.5 to 1.5 cm. in diameter, and pale gray areas of emphysema were present, mottling the smooth, glistening, pleural surface. Similar atelectatic and emphysematous areas were visible on section of the lung. Many of the bronchioles and smaller bronchi were conspicuous on section, due to the plugging of their lumina by white or yellow worm-like masses of stearate mixed with mucus and cellular detritus. The mucosa of the larger bronchi of the trachea was pale, but on its surface occasional masses of mucus, containing white flakes of stearate, were easily made out.

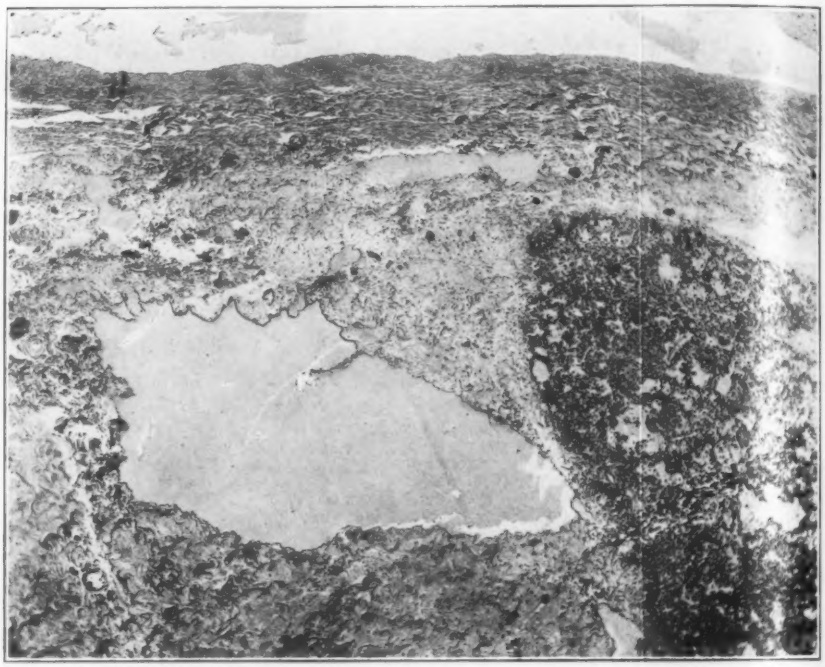


Fig. 5.—Dilatation of the lymphatics in the bronchial zone (× 50).

Microscopically, the gross picture described in the foregoing was confirmed. Areas of emphysema (Fig. 1) and atelectasis alternated (Fig. 2). Many alveoli, particularly the atelectatic ones, contained exudate—either a homogeneous pink material (precipitated serum) or a similar material in which red blood corpuscles, desquamated alveolar lining cells, and mononuclear cells were embedded. The alveolar walls in these zones of exudate were conspicuous on account of their increased size and the tortuous capillaries within them. Here and there, the alveolar epithelium formed a swollen, homogeneous, red band, devoid of nuclei. Many of the bronchioles were packed with leukocytes and with amorphous, blue-staining material (Figs. 3 and 4). The lining epithelium of these bronchioles seemed definitely thicker and proliferated. The vessels of the submucosa were dilated and surrounded by a small number of round cells. The lymphatics in the bronchial zones were greatly dilated and filled with a homogeneous or granular pink-staining material (Fig. 5). The subpleural

spaces, too, were much enlarged due to edema. They contained a similar precipitate. No other findings of importance were made.

SUMMARY

A child, aged 7½ months, died thirty-four hours after the inhalation of zinc stearate. Cyanosis and dyspnea characterized the clinical course of the illness, and a state of "acidosis" was noted after the patient was admitted to the hospital, twelve hours before death. At necropsy, the lungs were voluminous. Extensive areas of emphysema were separated from each other by small, scattered, atelectatic zones. The bronchioles contained plugs of zinc stearate and mucus, which appeared as wormlike masses. The gross picture was confirmed histologically, and the presence of extensive edema was determined. The edema involved the alveoli, especially the more atelectatic ones, and the subpleural and interlobular connective tissue septums. The lymphatics throughout the lung were conspicuously dilated.

In spite of oxygen inhalation, persistence of the dyspnea may have been due to acidosis brought about by incomplete obstruction to the bronchioles with zinc stearate.

DEFECTS IN THE MEMBRANOUS BONES, DIABETES INSIPIDUS AND EXOPHTHALMOS

REPORT OF A CASE *

BERNARD S. DENZER, M.D.
NEW YORK

This case is being reported, first, because of its rarity (only eight others are to be found in the literature) and, second, because thus far the condition has been observed only in children (the oldest patient reported was 16 years of age). The subject, therefore, may be of interest to the pediatrician.

REPORT OF CASE

R. L., a boy, when 4½ years of age, was operated on for removal of tonsils because of repeated attacks of sore throat. Two months after, the mother noticed small tender spots on the head, and because of that complaint the child was admitted to Mt. Sinai Hospital. The examination showed pallor, bad teeth, spongy gums and many soft spots on the head, the size of which was not mentioned. The Pirquet and the Wassermann reactions of the boy and the Wassermann reactions of the father and mother were all negative. The blood was not unusual; the amount of urine was normal and its examination was negative. The child was given the benefit of antisyphilitic treatment, although it was realized that the evidence pointed against syphilis. There was no improvement.

I saw the boy one year after the onset of the disease. The complaints at that time were thirst and the excretion of large amounts of urine, in addition to the persistence of soft spots on the head. Thirst and polyuria were only of about two weeks' duration. Examination showed a pale, stoop-shouldered boy with a slight but definite exophthalmos or, rather, proptosis. There was a soft spot about the size of the palm of the hand in the right occipital region, and a smaller spot over the left parietal bone. In these areas no bone whatsoever could be felt. The spot near the occiput bulged slightly and was quite tender; that in the parietal region was depressed and was less tender. The child passed from 6½ to 9 quarts of urine a day. The specific gravity varied between 1.000 and 1.004. Tests for albumin and sugar were negative. The blood count was normal.

The course of the disease could be followed for only six weeks. During that time subcutaneous injections of pituitary extract afforded only temporary relief of the urinary symptoms, and there was no change otherwise. The parents refused to permit hospital care and further study was impossible.

Seven other cases have been reported. These have been analyzed in an article by Grosh and Stifel [1] and the reader is referred to their paper for a complete and critical review. Therefore, I shall merely fill in the clinical picture with data from other cases.

---

* Received for publication, Nov. 3, 1925.

1. Grosh, L. C., and Stifel, J. L.: Defects in the Membranous Bones, Diabetes Insipidus and Exophthalmus with Report of Case, Arch. Int. Med. **31**: 76 (Jan.) 1923.

The onset in several cases was preceded by infection of the ear, throat or mastoid, and on the first examination spongy gums were also found. Otherwise, the histories give no clue to the etiology. The condition is not purely local, as indicated by the finding of similar defects in the pelvic bones. The only suggestion to be gleaned from the literature concerning prognosis is the statement of one of the German authors, that roentgenograms, taken six months after the first one, showed smaller lesions. Treatment with pituitary extract was uniformly unsatisfactory.

Light areas indicate defects.

In the most recently reported case in which there was necrospy performed, the authors conclude in part:

> In a case of defects in the membranous bones and exophthalmus studied clinically and pathologically, dyspituitarism as a cause for the syndrome was excluded by the absence of material pathologic changes in the hypophysis. . . From clinical behavior and pathologic findings an infectious etiology seemed more likely than a primary metabolic (endocrinologic) disturbance.[2]

COMMENT

The relation of the bone lesions to diabetes insipidus is interesting, and I have analyzed the reported cases in regard to this relationship.

2. Thompson, C. Q.; Keegan, J. J., and Dunn, A. D.: Arch. Int. Med. **36**:650 (Nov. 15) 1925.

The history of bone lesions either antedated that of diabetes insipidus or the bone defects were discovered coincident with the appearance of polyuria, a sequence of events which also indicates the antecedence of the defects in the bones. And, finally, in one case there was no polyuria.

In my case, a full year intervened between the discovery of the bone lesions and the appearance of polyuria. Chronologically, then, the bone defects seemed to be primary to the diabetes insipidus, and other considerations confirm that impression of the etiologic relationship. The list of the causes of diabetes insipidus includes brain tumor and any other condition which produces pressure on the hypophysis or the base of the brain. According to the work of Bremer and Bailey,[3] the hypothalamos and tuber cinereum (at the base of the brain), rather than the hypophysis, are the site of the lesion in diabetes insipidus. It requires little exercise of the imagination to assume that bone lesions which permit bulging at the occiput and depression at the vertex of the skull may distort the pressure at the base of the brain enough to disturb the function of centers situated there. This point of view that the bone defects are responsible for the diabetes insipidus, is not novel and has been suggested at least by Grosh and Stifel.

Exophthalmos also seems to be an incidental and not an essential lesion, due probably to a defect in the bones of the orbit.

163 West Eighty-First Street.

---

3. Bailey, Percival, and Bremer, Frederic: Experimental Diabetes Insipidus, Arch. Int. Med. **28**:773 (Dec.) 1921.

SYPHILITIC ENDARTERITIS IN CHILDREN *

HARRY M. GILKEY, M.D.
AND
C. C. DENNIE, M.D.
KANSAS CITY, MO.

Acute disease of the peripheral arteries is rare in children. It may be a sequel of an infectious disease, especially of typhoid, syphilis, pneumonia, influenza and rheumatism. It may follow trauma or result from embolism in the course of cardiac disease. The affected artery may become inflamed, with or without a consequent obliteration of its lumen. In the former case, unless rapid collateration circulation is established, gangrene of the parts supplied by the vessel results.

The symptoms in these cases consist of fever, swelling of the affected vessel, severe pain, numbness and tingling along its course, diminution of vascular pulsation, and if occlusion takes place, dry gangrene. In congenital syphilis, distinct changes have been found in the aorta and peripheral vessels and *Spirochaete pallida* have been demonstrated in the vascular coats.[1] In rare instances in infants, all the arteries are involved and the smaller vessels may be obliterated. The pathologic picture has been carefully studied by Wiesel,[3] who showed that the first change is infiltration of the media and vacuolation of the muscle layers. Later, the elastic tissue breaks up and the muscle fibers undergo necrosis. Spontaneous gangrene of the extremities is also described.[4] Aneurysm of the peripheral arteries is occasionally met in childhood. The most common causes are embolism and trauma.[5] Cautley has collected thirty-eight cases in subjects under 20 years, twenty-five of these being under 13 years. Males were affected twice as often as females. The locations of the aneurysms in this series were as follows:

Thoracic aorta, 6; abdominal aorta, 3; iliac, 1; femoral, 5; popliteal, 2; tibial, 4; carotid, 3; axillary, 2; innominate, coronary, ulnar, dorsalis pedis and cerebral, 1 each.

Two cases of syphilitic endarteritis with gangrene have been brought under our observation in the last two years.

---

* Received for publication, Nov. 7, 1925.

1. Rebaudi: Monatschr. f. Geburtsch. u. Gynäk. **35**:68, 1912.
2. Hale, White and Bryant: Proc. Roy. M. & Chir. Soc., Jan. 12, 1905.
3. Ztschr. f. Heilk.: **47**, 1906.
4. Khantz: Ztschr. f. Kinderh. **11**, 1914.
5. Diseases of Children, London, 1910.

REPORT OF CASES

CASE 1.—A girl, colored, aged 3 years, was admitted to the City Hospital, May 7, 1925. The day before admission, the mother noticed that there was a discoloration of the right foot which was not there the previous day. Previously the patient was apparently well, though always underweight, weighing at that time 14 pounds (6.4 kg.). The child was born at full term; the past history was negative.

Fig. 1.—Appearance of the right foot when the patient was first seen.

Fig. 2.—Large ulcer on right foot and leg.

On examination, the child was found to be undersized and poorly nourished, with bulging forehead and enlarged anterior cervical glands. The spleen and liver were both palpable 2 inches below the costal arch. With the exception of the lesion to be described, the physical examination was otherwise negative.

The entire dorsum of the right foot was of a bluish hue. The three middle toes and the ends of the great toe and little toe were black. On the plantar surface of the foot there was a large black bleb, extending about 2 inches backward from the three middle toes. The temperature of this foot was lower than the other, and no pulsation could be found in the popliteal space.

Laboratory Findings.—Urinalysis, negative. The red blood cells were 4,400,000; the white blood cells, 10,000. Hemoglobin, 80 per cent. Wassermann test, 4 plus.

CASE 2.—R. M., a girl, Mexican, aged 3 years, was brought to the Children's Mercy Hospital with a large ulcer on the outer aspect of the right leg, extending from the external malleolus for one-third up the leg. This lesion was covered with a black escharotic mass, which we at first thought due to contact with some powerful chemical. No history could be obtained from the parents because of their ignorance and inability to speak English. The child was well nourished and bore no outward stigmas of syphilis. The spleen, however, was palpable and the lower margin of the liver was 3 inches below the costal margin. On palpation, there was a moderate general adenopathy. Physical examination otherwise was negative, except for the ulcer described.

Laboratory Findings.—The Wassermann reaction of the blood was 4 plus; the cerebrospinal fluid was negative; the cell count—Lange colloidal gold—was normal.

Treatment.—Before the laboratory findings were obtained, wet dressings were applied to the ulcer for three days. The eschar sloughed off, exposing the tendon of the extensor peroneus muscle for 2 inches. The child was then placed on antisyphilitic treatment, complete healing of the ulcer resulting in four weeks' time. The tendon, which previously was exposed, was freely movable and covered with skin and subcutaneous tissue, with only moderate scar.

Each patient received the same type of treatment, namely, 0.15 gm. of neoarsphenamine intravenously every week for eight weeks. Potassium iodid was given internally.

COMMENT

It will be noted:

1. Both recovered promptly on antisyphilitic treatment.

2. In Case 1, there was loss of two toes. In Case 2, although the tendon was exposed, there was prompt and complete healing without ascending infection.

3. In both patients there was practically no pain or discomfort.

In endarteritis of nonsyphilitic origin, which produces gangrenous changes, the amount of destruction is nearly always greater and recovery is very slow. Therefore, we must conclude that syphilitic endarteritis involving the skin of extremities of children is more amenable to treatment than the ordinary type.

ERYTHEMA INFECTIOSUM *

A CLINICAL REPORT OF SEVENTY-FOUR CASES

THEODORE P. HERRICK, M.D.

CLEVELAND HEIGHTS, OHIO

Erythema infectiosum is described in practically all of the newer textbooks on pediatrics, but no clinical report of the occurrence of the disease in this country has been published previously. Most of the men who saw the cases reported in the present series felt that the disease was new in this locality, but several epidemics have been recognized elsewhere in recent years. Zahorsky [1] states that he saw a number of cases about 1914, and nine more cases during a localized epidemic in St. Louis in 1924. Shaw [2] quotes a personal communication from Dr. Brauer of Hamburg, N. Y., giving an account of thirty-seven cases which occurred in that town in the spring of 1919. The description of these cases leaves no doubt that they are the same condition reported in the German literature and in the present series.

The disease was accurately described as long ago as 1886 by Tschamer,[3] was first recognized as a distinct entity by Escherich [4] in 1896, and was given the name of erythema infectiosum by Stricker [5] in 1899. Other epidemics have been described by Gumplowiecz [6] in 1891, Tobeitz [7] in 1896, Schmidt [8] in 1899, Berberich [9] in 1900, Tripker [10] in 1901, Feilchenfeld [11] in 1902, Escherich [12] in 1904, Plachte [13] in 1904, Heimann [14] in 1904, Pospischill [15] in 1904, Michalowicz [16] in 1909, Heisler [17] in 1910, Tobler [18] in 1914, Weber [19] in 1916, and Ochsenius [20]

* Received for publication, Nov. 24, 1925.

1. Zahorsky, John: An Epidemic of Erythema Infectiosum, Am. J. Dis. Child. **28**:261 (Aug.) 1924.
2. Shaw: Abt's Pediatrics **5**:661.
3. Tschamer, A.: Jahrb. f. Kinderh. **29**:372, 1886.
4. Escherich, T.: Tr. Eleventh Internat. Med. Cong., 1896.
5. Stricker, G.: Ztschr. f. prat. Aerzte, **40**:121, 1899.
6. Gumplowiecz, L.: Jahrb. f. Kinderh. **32**:266, 1891.
7. Tobeitz: Arch. f. Kinderh. **25**:17, 1896.
8. Schmidt, A.: Wien. klin. Wchnschr. **12**:1169, 1899.
9. Berberich, E.: Inaugural Dissertation, Giessen, 1900.
10. Tripker: Kalender f. Frauen und Kinderarzte, kruznack, 1901.
11. Feilchenfeld, L.: Deutsch. med. Wchnschr. **28**:596, 1902.
12. Escherich, T.: Monatschr. f. Kinderh. **3**:285, 1904; Wien. klin. Wchnschr. **17**:631, 1904.
13. Plachte: Berl. Klin. Wchnschr. **41**:223, 1904.
14. Heimann, A.: Jahrb. f. Kinderh. **40**:421 (Feb.) 1904.
15. Pospischill, D.: Wien. klin. Wchnschr. **17**:701 (June) 1904.
16. Michalowicz: Jahrb. f. Kinderh. **71**:235, 1910.
17. Heisler: München. med. Wchnschr. **61**:1684, 1914.
18. Tobler: Berl. klin. Wchnschr. **51**:514, 1914.
19. Weber: Cor.-Bl. f. schweiz. Aerzte **46**:1453 (Oct. 21) 1916.
20. Ochsenius, K.: München. med. Wchnschr. **44**:838, 1917.

in 1917. Shaw [21] published the first American account in 1905, with colored illustrations, but it was the report of an epidemic observed abroad. The same author [2] gives a complete and up-to-date account in Abt's *Pediatrics*. Colored illustrations are available to English readers in Shaw's [21] article and in Feer's "Diagnosis of Children's Diseases."

SYMPTOMS AND CLINICAL COURSE

There are no prodromal symptoms. The first symptom is usually a dusky flush which appears on the cheeks, and is so sharply marked off that more than one parent described it as "a touch of erysipelas." Usually, close inspection at this time will reveal a few faint macular lesions around the neck at the base of the hair and some on the chin and forehead. Frequently this first stage is overlooked, and the first sign noticed is the second stage of generalized involvement. This may be quite faint or well marked and extensive. The rash is always more marked on the buttocks than on the trunk. This second stage lasts from several days to a week and passes gradually into the third stage, when the rash is limited to the arms and legs and the outlines persist for another week or longer. In some cases, recurrences lasting for several days were noted later in the summer. For convenience in description, a fourth stage might be included, consisting of a dusky mottling of the skin of the extremities, much like a faint cyanosis, which can be observed for several weeks following the disappearance of the rash.

While distinctly outlined, the rash on the face has a slightly irregular edge and is definitely raised, as a rule. This was usually the first symptom, but in some cases the rash on the face appeared late and was the most persistent manifestation.

The generalized rash is usually well marked and slightly papular on the buttocks. The upper part of the arms also usually show a papular rash. The trunk may be extensively involved with a rash which is definitely papular, but frequently there are only a comparatively few faint macules. When the rash is not well marked, the existence of any disease at this stage could easily be doubted.

The rash on the lower part of the arms merits more detailed description for several reasons; it may be the only manifestation of the disease noticed, the appearance there when typical could scarcely be confused with any other disease, and it is the easiest to observe when inspecting a schoolroom. The rash starts on the back of the forearm just above the wrist, and in the early stages cannot with absolute certainty be distinguished from sunburn. After a day or two it spreads farther toward the sides and up to the elbow, clear areas appear in the center, and the outline is more irregular and more distinctly marked off

21. Shaw: Am. J. M. Sc. **129**:16, 1905.

from the surrounding skin. The rash spreads peripherally, and small clear areas appear in the center which increase in size and coalesce, thus giving rise to the bright red irregular outlines typical of this stage. By the end of a week, the back of the arms will be clear except around the elbow and near the wrist, and the irregular outlines will have spread over the sides of the forearm to meet on the flexor surface.

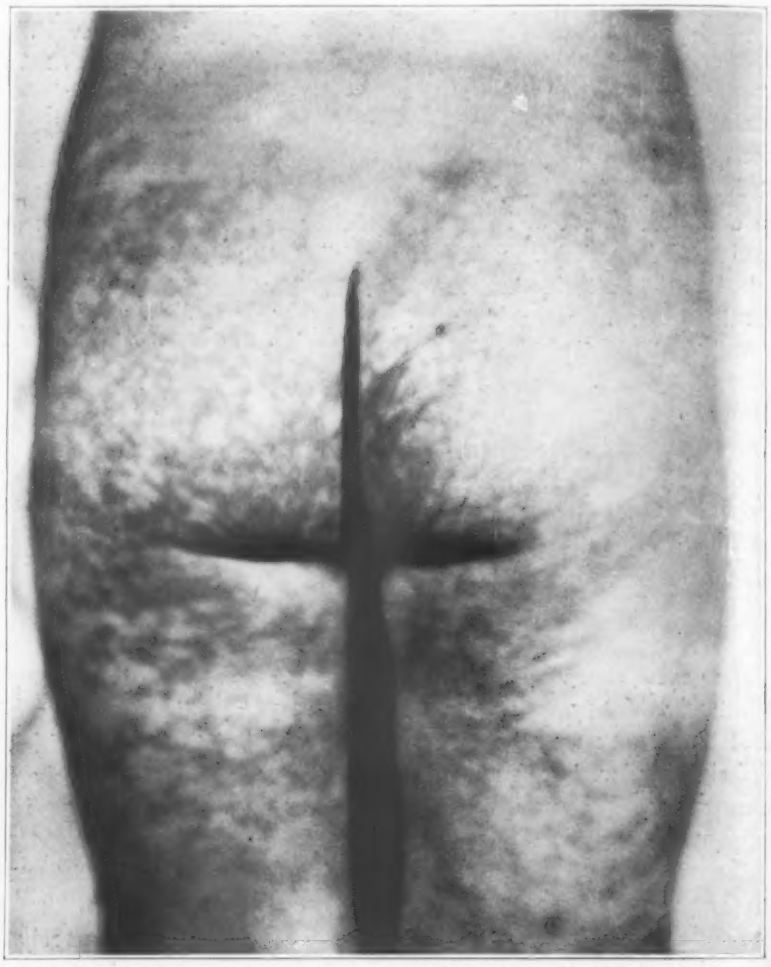


Fig. 1.—W. S. (case 52), buttocks on the sixth day, showing the second stage of generalized eruption. This and the following photographs were prepared by Dr. T. W. Todd, Department of Anatomy, Western Reserve Medical School.

When the rash is persistent, it spreads down over the back of the hand and may be distinctly seen on the proximal phalanx, but beyond that point it becomes fainter and is scarcely observable. These outlines were described by one mother as "lakes and rivers on a map," and they are the most distinctive feature of the disease.

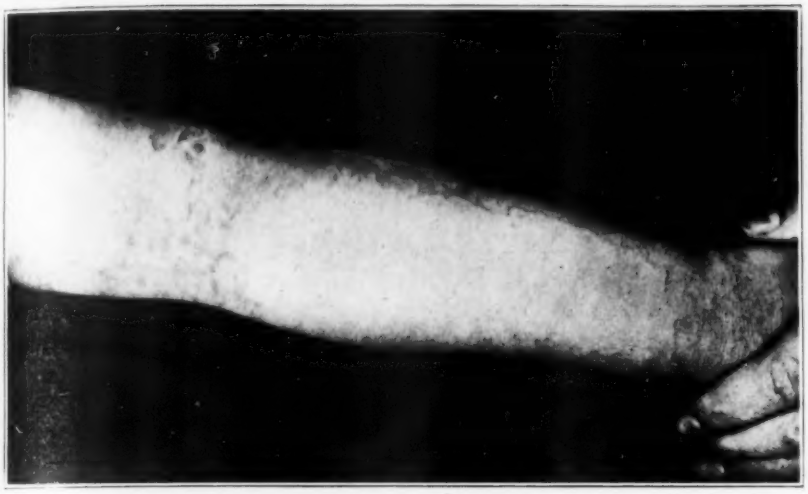


Fig. 2.—J. R. (case 44), left arm on the tenth day. The extensor surface, showing the clear area from which the rash has disappeared with the characteristic outlines at the periphery, and the typical distribution of the rash at this stage around the elbow, at the wrist, and on the flexor surfaces.

Fig. 3.—A. R. (case 45), the right forearm on the eighth day, the flexor surface, more extensive and more brilliantly outlined than usual; an extreme case but typical.

One characteristic feature is the evanescence of the rash at all stages, for it may disappear entirely only to reappear distinct and widespread some hours or days later.

ANALYSIS OF 1924 SERIES

This is based on fifty-two cases personally observed, but the number could have been nearly doubled if cases traceable through these children and those seen by other physicians were included. There were twenty-eight males and twenty-four females. All but four of the patients were between 6 and 15 years of age with an average of 9.4 years, but the susceptibility seems to be as great in younger children from the age of 1 year. The duration ranged from three to twenty-one days with an average of eleven days. In fourteen patients only, could any suggestion of symptoms other than the rash be discovered, and this was, at most, slight burning or itching and irritableness in the younger children. The one adult in the series said she felt quite miserable and that her arms ached. The contagiousness was fairly high. Of twenty-four families with two or more children, thirteen families had more than one patient.

It is an indication of the specificity of this disease that thirty-six of these children had had measles, six had rubella, and four had had scarlet fever. None of these patients desquamated or had any complications or sequelae. Throat and mucous membrane manifestations were lacking, as was also glandular enlargement. The lack of alarming symptoms is shown by the fact that of these fifty-two cases the family physician was called in only nine, and this was in a district in which the financial status is high, and the parents are educated to the importance of early diagnosis. Frequently the story was obtained that the mother had noticed the rash, put the child to bed and taken the temperature twice a day, but in the absence of rise of temperature or malaise, the physician was never called.

I have questioned at least three of the leading dermatologists of Cleveland, and none of them had ever seen a case of erythema infectiosum. Apparently, the mildness of the disease, so that a physician is rarely consulted, accounts for the lack of clinical reports in this country.

A summary of these cases will be found in Table 1.

CASES OBSERVED IN 1925

Twenty-two cases, comprised of four males and eighteen females were observed in 1925. No complete records were kept, but instead the attempt was made to find every case that occurred. The nurses and teachers were on the lookout, and the weekly inspections revealed scarcely any cases that had not already been reported. As this epidemic was

in a school system of over 5,000 children, the incidence in this year was not very high. An interesting feature is the relationship to the weather. Ten cases were observed at Fairfax School, Cleveland Heights, during a hot spell in the last week in April. May was a cold month, the rash died out in these subjects, and no new cases were observed at any

TABLE 1.—*1924 Cases*

Case	Date of Onset	Age	Sex*	Duration in Days	Order of Appearance of Rash	Remarks
1	May 2	10	♀	7	Arms, face, trunk.....	Irritable
2	3	13	♀	10	Arms, face, hands	
3	9	8	♂	10	Generalized	
4	31	10	♂	14	Generalized	
5	19	10	♀	10	Face, general.....	Face hot
6	June 11	10	♀	7	Arms.....	Very faint rash
7	12	10	♂	21	Arms	
8	May 5	9	♂	14	Arms	
9	5	12	♂	14	Trunk, limbs.....	Malaise
10	13	14	♀	28	Arms, legs.....	Hot, itched, recurred
11	June 24	12	♀	3	Arms.....	Itched
12	24	14	♀	3	Arms.....	Faint
13	May 16	11	♂	3	Face, arms, trunk.....	Rapid course
14	24	11	♂	14	Legs, arms, face, trunk	Itched, recurred
15	26	6	♂	16	Face, arms	
16	27	7	♀	14	Face, generalized	
17	June 4	7	♀	8	Generalized.....	Sleepy first day
18	9	8	♂	14	Face, arms	
19	10	11	♀	8	Arms.....	Mild
20	10	7	♂	7	General	
21	12	12	♂	14	Legs, general.....	Papular at first, later typical
22	12	8	♀	8	Arms, general.....	Malaise
23	13	8	♂	8	Face, arms, legs	
24	15	6	♀	14	Arms, general	
25	15	6	♀	14	Face, arms.....	Slightly papular
26	16	12	♂	14	Face, general, arms....	Itched
27	16	8	♂	7	Arms, face, general	
28	16	7	♀	10	Face, general.....	Definitely papular
29	16	9	♀	3	Face, arms.....	Light case
30	18	8	♀	7	Face, arms	
31	18	8	♂	8	Face, arms	
32	19	7	♂	14	General, face.....	Temperature 104 F. the first day (?)
33	20	9	♀	10	Face, body, arms	
34	21	9	♀	18	Face, general	
35	23	8	♀	14	Arms, general	
36	May 19	6	♂	14	Face, arms, legs	
37	June 21	9	♂	10	Arms	
38	19	5	♂	14	Face, arms.....	Irritable
39	20	7	♂	10	Face, general.....	Papular at first, typical recurrence
40	19	7	♂	7	Face, general.....	Irritable
41	22	8	♂	8	Face, general.....	Conjunctivitis slight
42	July 5	10	♀	7	Face, arms	
43	June 23	8	♀	21	Arms, face	
44	30	4	♂	21	Cheeks, arms, body	
45	July 2	15	♀	21	Arms, legs, back	
46	June 19	6	♀	14	Face, body	
47	July 1	9	♂	7	Face, general	
48	5	8	♂	3	Face, arms	
49	June 3	10	♂	10	Face, general	
50	15	1	♂	14	Face, general	
51	18	42	♀	10	Face, back, arms.....	Felt miserable, arms ached
52	July 7	3	♂	10	Face, general.....	Burning

* In this column, ♀ indicates female; ♂, male.

school for a full month. Then, after the warm weather beginning late in May, the condition was noted again at four other schools, and continued until the schools closed. During this second epidemic, no new cases appeared at Fairfax School, but in one of the earlier patients there was a brilliant recurrence on the arms and hands after a free interval of a month. Repeated inspections failed to reveal any cases at

Boulevarde School, which was the source of most of the cases observed in 1924. A chronologic summary of these cases by schools is given in Table 2.

LABORATORY DATA

Table 3 gives the results of blood counts made in seven cases, the complete counts being made for me by Dr. McGuiness, pathologist at Charity Hospital. Nothing in the blood examination offers any assistance in diagnosis.

TABLE 2.—*Cases Observed in 1925*

Case	Date of Onset	Fairfax	Roxboro	Coventry	Taylor	Roosevelt	Seen at Home
1	April 14	+	..	..	..	..	..
2	20	+	..	..	..	..	..
3	22	..	..	..	..	+	..
4	22	+	..	..	..	..	..
5	23	+	..	..	..	..	..
6	23	+	..	..	..	..	..
7	23	..	..	..	..	..	+
8	24	+	..	..	..	..	..
9	24	+	..	..	..	..	..
10	24	+	..	..	..	..	..
11	May 18	..	..	..	+	..	..
12	25	..	..	..	+	..	..
13	30	..	..	..	+	..	..
14	31	..	..	..	+	..	..
15	31	..	..	..	+	..	..
16	31	..	..	+	..	..	..
17	June 1	..	..	..	..	+	..
18	1	..	..	..	+	..	..
19	2	..	..	+	..	..	..
20	2	..	+	..	..	..	..
21	14	..	..	..	..	+	..
22	15	..	..	..	..	..	..

TABLE 3.—*Blood Examinations*

	Case	Date of Count	Day of Disease	White Blood Cells	Red Blood Cells	Hemoglobin	Differential
1924 cases	36	May 21	3	8,600			
	14	27	4	21,000	.....	..	Unexplained
	15	27	2	9,400			
	40	June 24	6	5,600	3,648,000	88	67-28-2-1-2
	41	24	3	5,700	4,000,000	85	62-34-2-1-1
1925 cases	8	April 28	5	20,400	.....	..	Acute cold
	5	29	7	7,400	5,024,000	..	56-34-6-2-2

No urine examinations were made, but the urine has been reported negative by other observers.

ETIOLOGY

The present series throws little light on the etiology; nose and throat cultures in several subjects showed nothing abnormal. The previous occurrence of the other exanthems and the character of the disease justify its consideration as a distinct entity. The occurrence of cases in the same room at school and the successive involvement of members of the same family can hardly leave any doubt of its infectious nature. The incubation period is difficult to determine, but the present series agrees

with other reports in giving from four to fourteen days, or possibly longer. So far as this series goes, it indicates a specific immunity; no patients who had the disease in 1924 were involved in 1925.

DIFFERENTIAL DIAGNOSIS

Of the nine subjects in this series who consulted the family physician, in only one, to my knowledge, was the correct diagnosis made. The most frequent explanation was a food rash (in several cases attributed to strawberries), or a toxic rash of unknown origin. Two of the 1924 series were reported to the Health Department as rubella, and at least one of the 1925 series was reported by the family physician as measles.

Rubella can be easily differentiated when the existence of such a disease as infectious erythema is known. The stage of general involvement may be similar except for the absence of enlarged posterior cervical glands in infectious erythema. The rapid progress and short duration of rubella is in marked contrast to the evanescent rash, lasting from ten days to two weeks.

Measles should easily be excluded by the absence of all the distinguishing features, namely, coryza, malaise, rise of temperature and Koplick's spots.

Scarlet fever can also be excluded by the absence of the characteristic symptoms, such as constitutional reaction, rise of temperature, angina, strawberry tongue, and desquamation.

Roseola infantum, when seen in the eruptive stage might be confused, but the history of several days preceding illness with rise of temperature and the more rapid fading of the rash distinguish it from erythema infectiosum.

Comparatively isolated cases of infectious erythema are likely to be included in the miscellaneous group of toxic rashes due to food, drugs, etc. This was the case even with physicians who knew of the existence of erythema infectiosum, until the occurrence of secondary cases put them on the right track. Only the occurrence of the other related cases or a case with a very typical course could make the diagnosis clear beyond a reasonable doubt.

Other diseases sometimes mentioned in the differential diagnosis are erythema exudation multiforme, pityriasis rosea, drug and serum rashes, urticaria, acrodynia or "pink disease," and the "fourth disease," but these should all be easily excluded by the history and the character of the rash.

TREATMENT

None is indicated. There is no evidence to show that anything is gained by keeping the children in bed or by changing the routine in any way. Isolation and quarantine might limit the spread of the disease,

but it would be impossible to enforce this, and fortunately the lack of serious symptoms or sequelae make such a course unnecessary.

SUMMARY

A series of seventy-four personally observed cases of erythema infectiosum is presented, and all the evidence in these cases indicates that the disease is a distinct entity, is infectious, and results in the establishment of a specific immunity.

The distinguishing features of the disease are its occurrence in epidemics, the lack of constitutional symptoms, the lack of any features distinctive of the other exanthems, the long course and characteristic progression of the rash, its evanescence at all stages, and particularly the irregular but brilliant outlines seen on the arms and legs in the third stage and in the recurrences.

SELECTED CASE HISTORIES

CASE 10.—A girl, aged 14, noted the onset of the condition on May 13, when the arms were red and hot, itched when washed but not at other times. The patient was seen on the third day, when a faint rash on the arms and forearms was noted. The seventh day, the rash was less marked, and was limited to the flexor surface of the forearms, around the elbows and the back of the hands. The ninth day, the rash was faint but definite on the lower part of the thighs and legs. The rash disappeared about the tenth day, but was observed again with a recurrence on the fifteenth day. Later, the patient stated that the rash recurred several times during the summer when brought out by sun or by heat.

CASE 18.—A boy, aged 8, noted the onset of the condition on June 9, with a flushed face and rash. (His mother stated that on June 3, his face was flushed and he had a slight rash under his ears, then this was better until June 9, when a rash was seen on arms.) Examination showed a marked mottled flush on the face, sharply delineated, a marked rash was typical on the extensor surfaces of the arms and forearms, thighs and buttocks, and slight on the lower legs. The second day the rash was less marked on the face, well marked on the buttocks, arms and legs, and slight on the chest. The third day, the rash was marked on the extensor surfaces of the forearms, and was slight on the hands and arms. The fourth day, the rash was marked on the arms, legs and buttocks, and faint but typical on chest. The fifth day, the rash was more marked on the flexor surfaces of the arms and forearms than elsewhere, and was still present on the legs. The eighth and ninth days the condition cleared up.

CASE 21.—A boy, aged 13, noticed a rash on the legs on June 12. When seen on the second day, there was a marked rash on the buttocks and thighs, which was reddish, slightly raised and like wheals. There was a marked raised eruption on the upper part of the arms, and a few lesions on the lower part of the arms. There was a slight but definite flush on the face. There was a typical mottled rash on the back of the neck, behind the ears, and a faint mottling on the trunk. On the third day, the rash behind the ears had gone, otherwise it was the same elsewhere. On the sixth day, there was a slight rash on the buttocks and legs, well marked on the upper arms, slight on the forearms, now less raised and more typical. On the seventh day, there was a marked rash on the upper arms and extensor surface of the forearms, and slight on the flexor surface; the rash was also present on the legs and buttocks; the face was clear. On the eighth day, the rash was faint but typical on the

flexor surface of the arms, forearms, buttocks, knees and calves. On the fourteenth day, there still were vestiges in the bend of the elbows and on the forearms, the lesions were few, but were typical and brilliant. One brother later had the disease.

CASE 24.—A girl, aged 6, noted the onset on June 15. When seen on the second day, the rash was typical in appearance, but was limited to the extensor surfaces of the forearms. On the third day, the rash was marked and typical on the extensor surfaces of the arms and forearms; it was slight on the buttocks and legs, and suggestive on the face and trunk. On the fifth day, the rash was marked and typical, with a large clear area on the extensor surface of both forearms surrounded by a mottled rash extending to the flexor surfaces, extending to the backs of the hands and fingers, and faintly on the palms, marked on the extensor surface of the upper arms, definite on the trunk, typical but not marked on the buttocks and outer side of the legs and marked on the calf of the legs.

CASE 38.—A boy, aged 5, noted the onset June 19. When seen on the first day, there was a faint but typical rash on the face and lower extensor surfaces of the forearms. On the seventh day, the rash was still typical on the face, less marked on the backs of the hands, and more extensive around the elbows and the knees. On the ninth day, it was faint but definite, and typical on the flexor surface of the forearms. On the twelve day, it was still seen on the flexors.

CASE 39.—A boy, aged 7, noted the onset on June 20. His face was flushed; on the second day, there was a papular rash, on the third day, erythema was visible but was never well marked. On July 3, the rash appeared again; when seen again on July 6, it was typical on the face and on July 19 the rash was definite on the upper arms. This was an atypical case. The patient was a brother of another patient (Case 38); two other children did not develop the condition.

CASE 51.—A mother of a family, aged 42, noted the onset on June 18; it was variable in appearance but was quite distinct on several occasions, especially on the thighs, arms, lower legs, back and face, the bright outlines often faded quickly. This patient had no elevation of temperature, but felt miserable, "like malaria" and her arms ached. The four youngest of six children had the disease.

THE RESPIRATORY METABOLISM IN INFANCY AND IN CHILDHOOD

III. GLYCOGEN STORAGE IN CHILDREN *

SAMUEL Z. LEVINE, M.D., JAMES R. WILSON, M.D.
AND
HELEN RIVKIN, M.A.
NEW YORK

This investigation was undertaken to study certain phases of the mechanism of glycogen storage in children. More specificially, it attempts to answer the following questions: 1. How much carbohydrate is mobilized for oxidation from the body stores of normal children during a given period of fasting under resting conditions? 2. Is the quantity different in children with cyclic vomiting under similar experimental conditions? 3. Does diabetes mellitus in children affect the capacity for glycogen storage?

A review of the literature reveals few previous attempts to measure accurately by means of the respiratory exchange the quantity of carbohydrate oxidized by children during fasting. Hasselbalch,[1] Bailey and Murlin [2] and Benedict and Talbot [3] independently observed high respiratory quotients in new-born infants during the first few hours of life, indicating the oxidation of stored glycogen. The rapid depression of the quotients thereafter signified an early exhaustion of the glycogen reserves. At the end of twenty-four to forty-eight hours, they reached the level of almost pure protein-fat combustion. Du Bois [4] interprets the results of Benedict's observations on fasting men,[5] as indicating that the body can utilize from 93 to 232 gm. of carbohydrate which have been stored away in glycogen depots. Richardson and Ladd [6] have shown by means of the calorimeter that adults with severe diabetes can mobilize

* Received for publication, Nov. 20, 1925.

* From the Department of Pediatrics, Cornell University Medical College and the New York Nursery and Child's Hospital.

1. Hasselbalch, quoted by Benedict: Respirationsforsøg paa nyfødte Børn, Bibliot. f. Læger **8**:219, 1904.

2. Bailey, H., and Murlin, J. R.: Energy Requirement of the New-Born, Am. J. Obst. **71**:526, 1915.

3. Benedict, F. G., and Talbot, F. B.: The Physiology of the New-Born Infant: Character and Amount of the Katabolism, Carnegie Inst. Washington Pub. No. 233, 1915.

4. Du Bois, E. F.: Basal Metabolism in Health and Disease, Philadelphia, Lea & Febiger, 1924, p. 25.

5. Benedict, F. G.: A Study of Prolonged Fasting, Carnegie Inst. Washington Pub. No. 203, 1915.

6. Richardson, H. B., and Ladd, W. S.: Clinical Calorimetry 34; Ketosis and the Respiratory Exchange in Diabetes, J. Biol. Chem. **58**:931 (Jan.) 1924.

considerable quantities of carbohydrate from the tissues for utilization during fasting. Richardson, Levine and Du Bois [7] found the same to be true in a case of severe hyperthyroidism.

METHODS

The apparatus and technic, methods of calculation, and the organization of the metabolism ward have been fully described in the first two papers of this series.[8] The quantities of protein, fat, and carbohydrate oxidized during fasting were calculated from the oxygen consumed, the carbon dioxid produced, and the nitrogen excreted in the urine in calorimeter observations of two to four hours duration. Respiratory quotients obtained over these periods were assumed to represent reliably the proportions of foodstuffs undergoing oxidation. The accuracy of the observations was controlled by means of frequent alcohol checks, the details of which are tabulated elsewhere.[8] Respiratory quotients in these checks ranged between 0.66 and 0.68 for two to three hour periods, and averaged 0.671 for all the determinations as against the theoretic quotient for alcohol of 0.667. If the correction for the error of + 0.6 per cent. in the average quotient be applied to the calculation of the maximum daily quantity of carbohydrate oxidized (154.7 gm. by L. A. [Case 3] on January 21), the error would be less than 1 gm., which is too small to introduce an appreciable error.

CASE HISTORIES

The group of children under investigation included two normal girls, one obese girl, one girl subject to cyclic vomiting, and one diabetic boy. The histories of the two normal children (Cases 2 and 3), the obese girl (Case 7), and the child with cyclic vomiting (Case 5) have been briefly given elsewhere (Cases 2, 3 and 7 in Paper 1 and Case 5 in Paper 2 respectively).[8] A more detailed account of the diabetic boy (Case 6 in Paper I) follows:

F. A., a boy, white, was born in the United States on Nov. 25, 1915. Symptoms of diabetes mellitus were first noted in February, 1925, including gradual loss of strength and excessive thirst. One month after the onset (March 6, 1925), sugar was discovered in the urine and insulin therapy was begun. With the aid of five units of insulin daily, the boy was finally able to tolerate a diet containing 1,800 calories. For the five days previous to admission on April 7, he was on this diet without insulin and glycosuria reappeared. The blood sugar on entrance was 158 mg. per hundred cubic centimeters. A three-day

7. Richardson, H. B.; Levine, S. Z., and Du Bois, E. F.: (To be published).

8. Levine, S. Z., and Wilson, J. R.: The Respiratory Metabolism in Infancy and Childhood. I. The Basal Metabolism of Children, Am. J. Dis. Child. **31**:323 (March) 1926. Wilson, J. R.: Levine, S. Z., and Rivkin, H.: The Respiratory Metabolism in Infancy and Childhood. II. Ketosis and the Respiratory Exchange in Children, ibid. **31**:335 (March) 1926.

period of fasting was instituted, followed by a diet which was gradually increased to 1,560 calories and 60 gm. of carbohydrate without insulin administration. The urine remained sugar-free following the initial fasting period except on one occasion when the daily carbohydrate quota of the diet was raised to 65 gm. The patient gained in weight and was free from symptoms. He progressed satisfactorily up to September 10, when he developed a mild upper respiratory infection, and, coincidently, his tolerance rapidly declined so that he was unable to utilize more than 20 gm. of carbohydrate daily without the appearance of sugar in the urine. With the subsidence of the infection, his tolerance did not return to the original level, and up to the time of writing (November, 1925), insulin therapy is required to enable him to tolerate a maintenance diet without glycosuria.

PLAN OF INVESTIGATION

The five children were studied during preliminary (storage) periods of high carbohydrate feeding and during subsequent fasting periods.

Storage Period.—In order to insure an adequate supply of carbohydrate for storage in the tissues, the children received high carbohydrate, high caloric diets for five to fourteen days preceding the commencement of the fasting periods. In the case of the diabetic boy (Case 6), the carbohydrate content of the preliminary diet was necessarily limited by his tolerance. This was found to be a maximum of 60 gm. daily. The total calories expended and the grams of carbohydrate oxidized by each child during these periods were determined directly in one or more calorimeter observations of two to three hours duration. During the calorimeter periods, the behavior of the children approximated that for the remainder of the day. From these data, the total caloric and carbohydrate requirements were computed. In four of the children the carbohydrate content of the storage diets exceeded the daily metabolic requirement as before calculated by at least 100 gm. However, the carbohydrate oxidized per twenty-four hours by the diabetic boy approximated the total 60 gm. contained in the daily diet. The protein content of all the diets was made adequate to cover the quantity metabolized, as determined from the nitrogen excreted in the urine. The fat intake always exceeded its daily oxidation.

The daily diet was divided into six equal portions and was given at four hour intervals. These small meals reduced the specific dynamic action of the ingested foods to a minimum. Furthermore, the children were kept in bed and their activity was markedly restricted. These precautions gave additional assurance that the calories and carbohydrate oxidized were maintained at levels sufficiently below the intake to insure in all the children except the diabetic boy saturation of the glycogen stores during the preliminary periods.

Fasting Period.—At the end of five to fourteen days, fasting was instituted, and in four children it extended for seventy-four to seventy-nine hours. In the fifth child (Case 3), the fast was terminated at the

end of fifty-five hours. The patients received only small, noncaloric meals, consisting of thrice-cooked 5 per cent. vegetables, agar-agar jelly and fat-free broth. Analyses of these articles from time to time demonstrated the absence of starch and sugar.

In an investigation of this type, the ideal procedure would have been to measure the respiratory exchange continuously throughout the fasting periods, and to prolong these periods to the point of complete depletion of the glycogen reserves. This procedure was unpractical. A method was substituted which reasonably approached this ideal. The children were strictly confined to bed throughout fasting periods. For the twelve to fourteen hours of the day during which they were awake, their activity was limited to writing, reading, sewing, and playing quietly with toys. Four to five calorimeter observations were made on each child at approximately equivalent hours during the progress of the fast. The children slept for the first one or two hours in most of the observations, and during the initial forty minutes of the last one or two hourly periods they duplicated as nearly as possible their activity for the remainder of the day during which they were awake. The children fell asleep or were kept absolutely quiet for the final twenty minutes of each active period in order to permit the respiration chamber to become stabilized before terminating the period. It may be assumed that the calorimeter results, when calculated for twenty-four hours, approximated the actual daily metabolism.

Furthermore, the proportions of foodstuffs oxidized during calorimeter periods probably represented reliably the proportions oxidized in the intervals between observations. Evidence for this belief is found in the similarity of the respiratory quotients obtained in equivalent experiments made at all times of the day and part of the night up to 12:10 a. m. Richardson and Ladd [6] also found no significant alteration of the quotient in two similar experiments on a diabetic patient, one being made in the afternoon and the other being repeated at midnight, thirty-six hours later.

Notwithstanding the necessary limitations of the method, we believe, for the reasons before enumerated, that it furnished a true measure of the total quantity of carbohydrate oxidized by the children during the short periods of fasting.

One of the objects of this study was to compare the relative quantities of carbohydrate oxidized by the different children during the same limited periods of fasting. It was, therefore, essential to subject them to as nearly equivalent experimental conditions as possible. In Table 1, the total heat production (obtained by taking an average of all the calorimeter results throughout the fasting periods) and the basal requirements of each child are compared.

The maintenance requirement of all the children ranged between 12 and 20 per cent. above their respective basal figures. Their relative activity, therefore, did not vary materially. In view of this, the experimental conditions were considered suitable for comparative purposes.

RESULTS

The details of the calorimeter observations are tabulated in a previous communication.[8]

Total Carbohydrate Oxidized During Fasting.—We have calculated from the calorimeter data the grams of carbohydrate oxidized per hour by the five children at approximately equivalent hours of fasting. The

TABLE 1.—*Effect of Restricted Activity on the Total Metabolism*

Case	Observations No.	Calories per Sq. M. per Hour * Maintenance Requirements Average	Basal Metabolism	Increase, per Cent
2	5	43.9	39.3	11.7
3	4	49.7	41.9	18.6
5	4	44.8	39.9	12.3
6	4	35.0	30.9	13.3
7	4	46.7	38.8	20.4

* Surface area obtained from Boothby diagram of Du Bois height-weight formula (Boston M. & S. J. **185**: 337, 1921).

TABLE 2.—*Grams Carbohydrate Oxidized Per Square Meter Body Surface During Fasting*

Case	Surface Area,* Sq. M.	Carbohydrates per Sq. M. Fasting Hours: 8 to 50 Gm.	8 to 74 Gm.
2	0.89	153	192
3	0.735	144	...
5	0.785	155	196
6	1.015	92	135
7	1.16	145	201

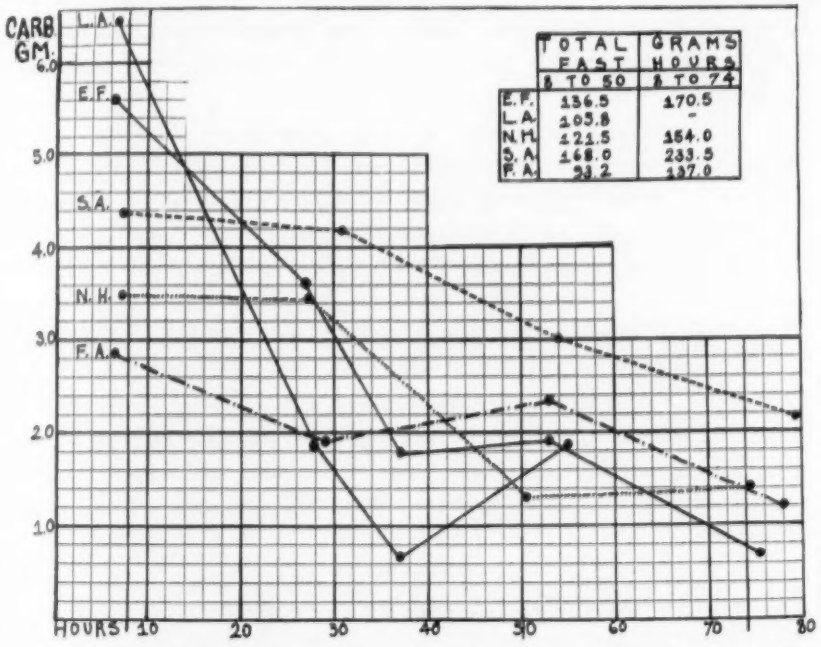
* Surface area obtained from Boothby diagram of Du Bois height-weight formula (Boston M. & S. J. **185**: 337, 1921).

results appear in the chart. If we accept the assumption that fluctuations in the total and carbohydrate metabolism were insignificant in the intervals between observations (the justification for this assumption has been discussed in the foregoing), the total grams of carbohydrate oxidized throughout the entire periods of fasting may be calculated from the chart. These quantities are tabulated in the upper right corner. They differ quite markedly in the five children.

By using the surface area as a basis for comparison, the relative quantities of carbohydrate oxidized by all the children with the exception of the diabetic boy were strikingly similar (Table 2). In the

interval between eight and fifty hours of starvation, the first four children oxidized from 144 to 155 gm. of carbohydrate per square meter of body surface; between eight and seventy-four hours of fasting they oxidized 192 to 201 gm. per square meter. The carbohydrate oxidized by the diabetic boy (Case 6) during equivalent periods of fasting was notably lower, being 92 and 135 gm. per square meter respectively.

It is of interest to point out that the decline in the sugar content of the blood from the beginning to the end of the fast was approximately



Grams of carbohydrate oxidized per hour by the five children during fasting as determined from the calorimeter data. In the upper right corner are given the total grams of carbohydrate oxidized in the intervals between eight and fifty hours and eight and seventy-four hours, respectively, as computed from the graph.

the same in four of the five children. In them, the total decrease equalled 16 to 25 mg. per hundred cubic centimeters. In the fifth child (Case 3), the blood sugar fell 64 mg. per hundred cubic centimeters. In view of this relatively small and approximately equal drop in the blood sugar, it may reasonably be assumed that the glycogen stores of the body were the principal source of the carbohydrate oxidized by at least four of the five children.

The results show that under maintenance conditions normal children, irrespective of their state of nutrition, as well as the patient with

cyclic vomiting, oxidized relatively similar quantities of mobilized carbohydrate during equivalent periods of fasting. The diabetic boy metabolized carbohydrate up to the limit of his tolerance during the preliminary period. The nature of the disease made it impossible to feed carbohydrate sufficiently in excess over the quantity metabolized to afford an adequate supply for storage.

SUMMARY

1. By use of the respiration chamber, absolute and comparative measurements of the total carbohydrate oxidized by five children during short periods of fasting were made. The necessary limitations of the method and the reasons for accepting it as satisfactory have been discussed.

2. Under similar conditions—the total metabolism of all the children ranged between 12 and 20 per cent. above their respective basal requirements—two normal girls, one obese but otherwise normal girl, and one girl subject to cyclic vomiting, oxidized approximately equal quantities of carbohydrate per square meter of body surface during equivalent fasting periods. They utilized from 144 to 155 gm. and from 19- to 201 gm. of carbohydrate per square meter in the intervals between eight and fifty hours and eight and seventy-four hours respectively.

3. Under the same conditions, except for a reduced carbohydrate content in the storage diet, and for the same duration of fasting, one boy suffering from a moderate form of diabetes mellitus metabolized considerably smaller quantities—92 and 135 gm. per square meter, respectively.

CONCLUSIONS

1. The fact that the glycogen deposits are replenished (glycogenesis) during high carbohydrate feeding, and that carbohydrate is mobilized for oxidation (glycogenolysis) during starvation is confirmed.

2. The experimental conditions were not suitable for making quantitative measurements of the comparative efficiency of glycogen formation in the group of children studied. The results clearly demonstrate, however, that glycogen was adequately formed in the patient with cyclic vomiting. If these results are found to apply to other children suffering from the same condition, they would imply that a diminished capacity for glycogen formation is not a factor in the hypersusceptibility of these children to ketosis.

3. A defective mechanism of glycogen formation was a factor in producing the low tolerance for carbohydrate present in the boy with diabetes mellitus.

4. Under maintenance conditions, the relative quantities of carbohydrate mobilized from fully replenished stores and oxidized during short periods of fasting are approximately the same in normal children, irrespective of their nutritional state.

5. Between attacks and during resting conditions, the quantity was not diminished in the patient with cyclic vomiting. As indicated from the data of one case, defective glycogenolysis does not apparently explain the exaggerated tendency of these children to ketosis.

Further work on additional patients with cyclic vomiting and diabetes mellitus is planned, in which the duration of the fasting periods will be lengthened.

URIC ACID AND CREATININ IN THE URINE OF INFANTS *

O. S. ROUGICHITCH, M.D.
BOSTON

URIC ACID

Medical literature abounds with publications concerning the uric acid excretion and its variations in relation to diet and to conditions of health and disease. Pediatric literature, however, gives but little information on the excretion of uric acid by infants. This is due chiefly to the difficulties encountered in collecting the infant's urine quantitatively. The published data we have found are summary and incomplete, and are often contradictory. The discrepancies apparent are probably referable to inaccurate measurements. Until quite recently, the methods for determining uric acid have not been satisfactorily dependable.

We find that Lesné and Binet,[1] in their publication, state that one can find 0.15 gm. of uric acid excreted in the urine of infants in twenty-four hours. They reported the figures of Kotscharowsky, showing the relationship between urinary uric acid and urea in the new-born and during the first months of life. These are seen in Table 1.

Orgler [2] states that the uric acid output in artificially fed infants is higher than in breast fed infants, and ascribes as the reason for this difference the better utilization of food by the latter. In 1922, K. Utheim [3] published her observations on thirty infants, most of them athreptic and a few normal. She found in her cases that the variations in the uric acid excretion were large, between 1.5 and 40.0 mg. per kilogram of body weight per twenty-four hours, and that there seemed to be no relationship between the uric acid excretion and the nutritional condition of the infant. Recently, Leopold, Bernhard and Jacobi [4] studied the uric acid output in five children under varying conditions and different diets. The most important of their findings was that a high protein diet results in a greater uric acid elimination up to a certain point, after which, with protein intake further increased, the rate of uric acid

* Received for publication, Nov. 13, 1925.

* From the laboratory of the Department of Pediatrics, the Harvard Medical School and the Wards of the Infants' Hospital.

1. Lesné, E., and Binet, L.: Physiologie Normale et Pathologique du Nourrisson, Paris, Masson & Cie., 1921.

2. Orgler: Jahrb. f. Kinderh. **67**:383, 1908.

3. Utheim, K.: Metabolism Studies in Infants Suffering from Chronic Nutritional Disturbances, Am. J. Dis. Child. **22**:329 (Oct.) 1921.

4. Leopold, J. S., Bernhard, A., and Jacobi, H. G.: Studies in the Uric Acid Metabolism of Children, Am. J. Dis Child. **27**:243-255 (March) 1924.

elimination decreased. This they explained as due to "kidney fatigue." [5] Contemporarily, Folin, Berglund and Derick [6] published extensive studies on uric acid metabolism and demonstrated that more endogenous uric acid is excreted on a high protein diet than on low protein diets.

It has been shown that the uric acid found in the urine is the end-product of the catabolic processes of the nucleoproteids from ingested food, as well as those from the body tissues. To Burian and Schur [7] belongs the credit of being the first to distinguish clearly these two sources of the uric acid, that is, exogenous and endogenous. Because their food regimen is normally purin free, the uric acid eliminated by infants represents the endogenous uric acid. It is therefore with uric acid from this source that we are concerned in this study.

The infants from whom the data here given were obtained were patients in the wards of the Infants' Hospital. As the method for col-

TABLE 1.—*The Relationship Between Uric Acid and Urea in the New-Born and During the First Months of Life*

Age	Uric Acid : Urea
1 day	1: 7.9
2 days	1: 8.0
3 days	1:12.2
4 days	1:12.9
5 days	1:18.8
6 days	1:19.3
20 days	1:50.2
40 days	1:42.5
80 days	1:31.0
Adult	1:70.0

lecting the urine is applicable only to the male infants, all of them were males. The majority were being treated for "regulation of feeding," and in no instance was there any evidence of recent disturbances of digestion. In some instances our subjects were nearly normal as regards nutritional condition; in others they were undernourished and underweight, and a few of them were premature. In most instances the diet was cow's milk, almost invariably in the form of lactic acid milk, with fat, carbohydrate and protein percentages varied according to the needs of the infants. A considerable period on a given diet preceded the collection of urine specimens. A few older infants were on a mixed diet but purin free; their regimen consisted of milk as a basis, with the addition of eggs, junket, custard and carbohydrates. All the infants were weighed daily, and the reported weights are the average of their body weight during the two periods of study.

5. Leopold, J. S.; Bernhard, A., and Jacobi, H. G.: Further Studies in the Uric Acid Metabolism of Children, Am. J. Dis. Child. **29**:191-199 (Feb.) 1925.

6. Folin, O.; Berglund, H., and Derick, C.: J. Biol. Chem. **69**:361-471 (June) 1924.

7. Burian and Schur: Arch. f. d. ges. Physiol. **87**:239, 1908.

The urine collections were carefully observed, and our report deals only with the accurate collections. The urine was preserved during the collection in a container surrounded by ice; toluene was added to the urine specimens at the end of the periods. The infants were immobilized by means of a comfortable metabolism frame in use in this hospital in which they seemed happy. In some instances there was slight regurgitation or vomiting, possibly due to the continued horizontal position and immobility of the infant for feeding. The collection periods were of twenty-four hours' duration and the urine was analyzed immediately after each period. The uric acid determinations were made by the microchemical colorimetric method of Folin and Denis.[8] Total nitrogen was determined by the Kjeldahl method. Table 2 gives the data obtained.

These figures show a surprisingly high value for uric acid excretion in the cases studied. If we compare the urinary end-products of endogenous purin metabolism in adults and in our infants, we find that it is several times higher in the latter. Burian[9] gives from 0.30 to 0.60 gm. of endogenous uric acid output in twenty-four hours as an average for an adult. In our cases the uric acid elimination averages from 15 to 20 mg. per kilogram of body weight per twenty-four hours, consequently from three to four times higher than in adults.

That the urine of infants is rich in urates is commonly known, as is also the frequency of uric acid infarcts in the kidneys taken postmortem from new-born and from premature infants. Urates in the urine of infants are seen as fine, red crystalline deposit on the diapers; uric acid calculi are frequently observed clinically. From where does this relatively large amount of uric acid appearing in the urine come? It is, perhaps, reasonable to postulate a larger production of endogenous uric acid in infants as a consequence of the more rapid rate of metabolic processes during this period of life. It is possible, however, that another factor is concerned in this larger excretion of uric acid by infants. It is at present believed that uric acid elimination by adults represents only a part of the total production of this substance, a larger part being destroyed and probably converted into urea by some unknown mechanism. Using this conception, the relatively large uric acid excretion by infants may be due to a lesser destruction of endogenous uric acid, and should represent more nearly the actual quantity of uric acid produced than in the case of adults. The possibility of this explanation is based on the following published data.

---

8. Folin, O.: Laboratory Manual of Biological Chemistry, New York, D. Appleton & Company, 1923.

9. Burian: Footnote 7.

TABLE 2.—*Uric Acid Output in Twenty-Four Hours*

Case	Age, Mo.	Weight, Kg.	Food Calories	Date	C.c. Urine	Mg. Total Nitrogen	Mg. of Total Uric Acid	Mg. Uric Acid per Kg. Body Weight	Admitted for
1	2	4,354	Lactic acid milk mixture, 410	6/27 6/28	282 420	997.5 1,047.2	86.7 84.0	19.9 19.3	Acute digestive disturbances
2	7	7,037	Whole lactic acid milk, 600	6/19	415	2,039.8	112.5	16.0	Double otitis media
3	11	9,610	Whole milk, 726	8/ 7 8/ 8	560 757	4,173.1 3,901.1	192.9 196.0	20.1 20.4	Slight convulsions of unrecognized origin
4	22	10,952	Mixed diet	7/ 8 7/ 9	260 257	4,571.0 5,256.8	214.0 207.2	19.0 18.9	Bronchopneumonia convalescent
5	20	9,586	Mixed diet, 693	7/23 7/24	445 648	3,603.6 4,023.8	158.7 168.0	16.5 17.5	Ferriprive anemia
6	1	2,948	Lactic acid milk mixture, 370	6/25 6/26	383 445	728.0 819.0	61.7 64.0	20.0 21.3	Regulation of feeding
7	1½	3,374	Whole milk mixture, 326	7/24 7/25	230 102	881.1 611.5	69.3 74.3	20.5 21.0	Regulation of feeding
8	2	2,606	Lactic acid milk mixture, 340	6/29 6/30	213 330	687.9 770.5	55.5 62.1	21.2 23.8	Prematurity
9	3	4,142	Lactic acid milk mixture, 500	7/16 7/17	330 325	1,724.8 1,552.6	158.1 141.4	35.7 34.1	Active rickets
10	5	3,800	Whole milk mixture, 480	7/ 1 7/ 2	380 498	1,235.3 1,582.0	61.7 65.0	16.7 17.1	Regulation of feeding
11	5	4,394	Lactic acid milk mixture, 560	7/18 7/19	225 225	913.9 928.8	109.9 106.5	25.0 24.2	Otitis
12	5	4,764	Lactic acid milk mixture, 440	6/27 6/28	195 250	1,581.3 1,524.4	81.6 88.5	17.1 18.5	Otitis
13	6	5,952	Lactic acid milk mixture, 390	7/15 7/16	140 137	1,278.8 1,510.0	129.0 136.0	22.8 21.6	Acute gastro-intestinal disturbances
14	6½	3,060	Lactic acid milk mixture, 290	7/26 7/27	295 410	997.5 969.8	64.3 70.5	21.0 22.0	Regulation of feeding prematurity
15	8	2,026	Cow's and breast milk, 180	7/ 4 7/ 5	96 127	435.4 406.0	29.0 38.7	14.0 18.8	Harelip
16	12	6,040	Mixed diet, 695	7/ 1 7/ 2	445 420	2,073.1 2,503.2	94.2 111.2	15.6 18.4	
17	15	6,154	Whole milk, 720	7/10 7/11	430 352	3,234.0 2,663.0	123.7 121.2	20.1 19.3	Secondary anemia
18	17	8,766	Mixed diet, 1,000	7/ 4 7/ 5	382 376	3,787.5 3,885.0	227.0 175.4	24.7 20.0	
19	21	9,590	Mixed diet, 785	7/13 7/14	235 270	4,746.0 3,945.2	233.0 175.0	24.2 18.2	Convulsions of unrecognized origin
20	1½	2,950	Lactic acid milk mixture, 360	7/25 7/26	385 522	660.8 868.5	68.8 62.2	23.2 21.0	Prematurity
21	1¾	2,382	Breast milk, 240	7/18 7/19	105 158	117.0 127.7	32.9 34.5	13.8 14.4	Prematurity
22	2	3,800	Lactic acid milk mixture, 405	7/14 7/15	250 230	1,104.0 1,218.0	58.8 63.5	15.4 16.7	Prematurity

Contrary to the opinion previously accepted, that the rate of endogenous uric acid excretion, being constant and varying only according to individuals, is in no way affected by a high protein intake, Folin [10] first, then Lambling and Dubois,[11] and then Höst,[12] demonstrated that the high protein purin free diets promote the elimination of the endogenous uric acid. In a recent extensive work, Folin returns to this subject, and with his co-workers Berglund and Derick [6] finds confirmation of his opinion by further experiments. They conclude that the higher endogenous uric acid output, on a purin free high protein diet is due to an accelerated elimination and reduced destruction, but not higher production. They consider that the higher protein diets increase the responsiveness of the kidney and thus lower the level of circulating uric acid and that, because of those lower levels less uric acid is destroyed and consequently more is eliminated.

Returning to the data from the infants here studied, it may be seen that their food regimen corresponds exactly to Folin's just mentioned experimental conditions. In no period of human life is the protein intake so high as at this early age. Although the protein intake of a breast fed infant is high, it is still higher in the case of the artificially fed. A probable explanation of the high uric acid output by infants is thus indicated. In satisfactory agreement is the somewhat lower excretion by breast fed infants, as stated by Orgler and as found in our two cases.

As before mentioned, the hitherto reported measurements of uric acid excretion by infants indicate a variability which is surprisingly wide when it is considered that the infants' diet is purin free. It was the chief purpose of this study to observe the degree of regularity of the uric acid output, using all possible care in the collection of twenty-four hour specimens and a recently devised and very accurate uric acid method. As may be seen in Table 1, the day by day excretion of uric acid is closely constant for the individual infant. Comparing the measurements from different infants, the uric acid output is, in this series of subjects, usually a fairly constant value. The extreme limits here found are from 13.8 to 25.0 mg. per kilogram of body weight. No definite relationship between the age of the infant and the excretion of uric acid per kilogram of body weight is apparent from these data. We note without commentary that in the case of the infant with acute rickets, the uric acid excretion was as high as 35.7 and 34.1 mg. per kilogram of body weight in twenty-four hours. Except in this instance, uric acid excretion does not seem to be affected by differences in nutritional state. As might be expected, uric acid output is found to be

10. Folin, O.: Am. J. Physiol. **13**:66, 1905.
11. Lambling, E., and Dubois, C.: Compt. rend. Soc. de biol. **76**:614, 1914.
12. Höst, O.: J. Biol. Chem. **38**:17 (May) 1919.

quite independent of the quantity of urine produced. For instance, one infant (Case 4) voided 260 c.c. of urine containing 214.0 mg. of uric acid, whereas the urine volume for another infant (Case 10) was 498 c.c. and the uric acid content only 65.0 mg. The relationship between the total urinary nitrogen and the uric acid nitrogen varies, according to our data, from 1.25 to 3.5 per cent. for uric acid nitrogen. This percentage for uric acid nitrogen is seemingly low, but our patients were artificially fed, and consequently had a higher total nitrogen output as compared with normal breast fed infants.

CREATININ

In studying the urinary end-products of the endogenous nucleoprotein metabolism of our subjects, we simultaneously undertook to determine their urinary creatinin excretion, as an index of their endogenous protein metabolism.

We find in the literature more established facts about this nitrogenous constituent of urine in infants, than is the case of uric acid. Funaro [13] finds that the creatinin urinary excretion in infants per kilogram of body weight in twenty-four hours varies between 4.62 and 10.81 mg. He does not think that excretion was affected by diet or by the nutritional condition of the infant. Lesné, Binet and Deffins, on the basis of a study of thirteen infants in different age groups and nutritional conditions, state that the elimination of creatinin bodies increases with the age of the infant, being 1.3 to 3.0 mg. per kilogram of body weight during the first days of life, rising to 4.0 to 5.0 mg. at 2 months and to 19.0 mg. at 24 months, thus attaining at that age the figure for adults. K. Utheim,[14] in 1922, studied nineteen cases, two of which were normal, the others in various morbid conditions, and most of them athreptic. The two normal infants gave 9.1 and 10.5 mg. of creatinin per kilogram of body weight in twenty-four hours, the others ranging from 3.0 to 13.0 mg. Her figures for infants in very poor nutritional condition were somewhat lower.

The origin and significance of creatinin in the urine, in spite of numerous studies, has not yet found a satisfactory explanation. In the case of infants, this problem is still more obscure, since their creatinin metabolism seems to be quite different from that of adults and their urine also yields large amounts of creatin. Gamble and Goldschmidt [15] have shown that creatin ingested by infants appears nearly completely in the urine. This is not the case with adults, and they infer that the infant has much less ability to destroy or to transform creatin. They

13. Funaro: Biochem. Ztschr. **10**:467, 1908.
14. Utheim, K.: Footnote 3.
15. Gamble, J. L., and Goldschmidt, S. J.: J. Biol. Chem. **40**:199 (Nov. 1) 1919.

also demonstrated that the creatin excretion of infants can be increased by increasing the intake of milk. They showed that this result is not due to an increase of protein intake by obtaining the same result with cream and whey mixtures, and infer that it is explained by the presence of preformed creatin in solution in the milk whey. They also demonstrated a slightly higher excretion of creatinin on a whole milk or on a cream and whey diet, than was the case when diluted cream was given. Folin's discovery, that creatinin excretion is closely constant for the person and proportional to his body weight and muscular development and independent of protein intake, remains the most significant finding in this field.

The creatinin determinations here given were obtained from the same infants as were the uric acid measurements, consequently we deal with the same conditions as to the normality of cases, diet, and technic of collection and preservation of the urine. The determinations of creatinin were by the colorimetric method of Folin.[16] Our results are given in Table 3.

From Table 3, it may be seen that there is a close relationship between the body weight and daily creatinin excretion in our cases. In the case of all of our infants, regardless of difference in age and nutrition, our figures for creatinin output range between 10.2 and 15.9 mg. per kilogram of body weight in twenty-four hours. These figures are practically identical with those of the before-mentioned authors, except that for younger infants they are somewhat higher, and that, in general, the individual differences are rather smaller. One of the interesting features of our table is that the higher figures for creatinin excretion were obtained in the cases of infants in poorer nutritional condition possibly indicating a higher "wear and tear" quota for their tissue metabolism, but more probably the result of a relatively larger mass of active protoplasm per unit of body weight in thin infants. Our results substantiate the conception that under usual circumstances of metabolism the excretion of creatinin is a closely constant value per unit of protoplasmic mass. That this unit is not accurately parallel with body weight in a group containing fat and thin infants probably explains to a considerable extent the range found. It is possible that the differences in the amount of milk fed, representing, according to Gamble and Goldschmidt, small but differing amounts of preformed creatinin, may also be a factor.

EFFECT OF MUSCULAR ACTIVITY ON CREATININ EXCRETION

The influence of activity of the skeletal muscles on creatinin excretion has been suggested by many authors, and it was found that the creatinin output in adults was lower during the night period of sleep than during

16. Folin, O.: J. Biol. Chem. **17**:469, 1914.

the day. To find out whether this was true in our cases, we carefully observed the infants and noted the extent to which they slept during each period. The differences in sleeping-time in different periods being very small—one or two hours—in the majority of cases, we could not find evidence to justify any such conclusions therefrom. It seems worth while to mention that in the case of a few infants, who slept from

TABLE 3.—*Creatinin Output in Twenty-Four Hours*

Case	Age, Mo.	Weight, Kg.	Food	Date	C.c. Urine	Mg. Total Creatinin	Mg. Creatinin per Kg. Body Weight	Admitted for
1	2	4,354	Lactic acid milk mixture	6/27	282	47.3	10.8	Acute digestive disturbances
				6/28	420	54.0	12.3	
2	7	7,037	Whole lactic acid milk	6/19	415	82.5	11.7	Double otitis media
3	11	9,610	Whole milk	8/ 7	560	108.0	11.2	Slight convulsions of unrecognized origin
				8/ 8	757	104.5	10.8	
4	22	10,952	Mixed diet	7/ 8	262	142.1	12.9	Bronchopneumonia convalescent
				7/ 9	250	132.8	12.1	
5	1	2,948	Lactic acid milk mixture	6/25	383	34.2	11.5	Regulation of feeding
				6/26	445	42.8	14.4	
6	1½	3,374	Whole milk mixture	7/24	230	45.2	13.3	Regulation of feeding
				7/25	102	44.1	13.0	
7	2	2,606	Lactic acid milk mixture	6/29	213	39.3	15.0	Prematurity
				6/30	330	36.4	14.0	
8	3	4,142	Lactic acid milk mixture	7/16	330	65.2	15.7	Active rickets
				7/17	325	63.0	15.4	
9	5	4,394	Lactic acid milk mixture	7/18	225	67.5	15.3	Otitis
				7/19	225	64.8	14.7	
10	5	4,764	Lactic acid milk mixture	6/27	195	48.8	10.2	Otitis
				6/28	250	55.6	11.6	
11	6	5,952	Lactic acid milk mixture	7/15	140	63.9	10.7	Acute gastro-intestinal disturbances
				7/16	137	72.0	12.0	
12	6½	3,060	Lactic acid milk mixture	7/26	295	48.8	15.9	Regulation of feeding, prematurity
				7/27	410	48.4	15.8	
13	8	2,026	Breast milk	7/ 4	96	25.3	12.3	Harelip
				7/ 5	127	27.0	13.3	
14	12	6,041	Whole milk	7/ 1	445	76.3	12.6	
				7/ 2	420	78.4	13.0	
15	15	6,154	Whole milk	7/10	430	88.1	14.4	Secondary anemia
				7/11	252	83.6	13.5	
16	17	8,766	Mixed diet	7/ 4	382	102.1	11.6	
				7/ 5	376	98.0	11.1	
17	1½	2,950	Lactic acid milk mixture	7/25	385	34.3	11.6	Prematurity
				7/26	522	39.6	13.4	
18	1¾	2,382	Breast milk	7/18	105	29.0	12.1	Prematurity
				7/19	158	27.2	11.3	
19	2	3,800	Lactic acid milk mixture	7/14	250	52.6	13.8	Prematurity
				7/15	230	52.0	13.6	

eighteen to twenty out of twenty-four hours, the creatinin output was not lower than it was in the case of infants who slept half of that time. A few of the infants were markedly hypertonic, but the data obtained in studying them did not show any definite effect of muscular hypertonicity on their creatinin excretion. However, the results in the following cases are interesting:

REPORT OF CASES

CASE 1.—S. I., a boy, aged 21 months, weighing 9.59 kg., was admitted to hospital on July 10, on account of convulsions, the cause of which was not definitely known. The past history of the infant was essentially irrelevant; his birth was normal, and delivery easy; he made good gain since birth; and was breast fed for six months; he had frequent convulsions since the sixth month, particularly when angered. Two days before admission, the infant developed fever and diarrhea; he became quite restless and had vomited for the past two mornings. His convulsions were quite frequent and were easily precipitated. The patient was a hypertonic, pale boy, who gave definite evidence of rickets as shown by large parietal bones, rachitic rosary and enlarged wrists. The convulsions seemingly were typical of tetany. The reflexes were hyperactive and Chvostek's sign was questionably present. Trousseau's sign was not obtained. The findings otherwise were normal, except for palpable axillary, inguinal and cervical lymph nodes. At 5 p. m. the day of admission he was put on the metabolism frame, and the urine was collected for nine hours. During the

TABLE 4.—*Creatinin Excretion of Case 1*

July	Body Weight	C.c. Urine	Mg. Total Creatinin	Mg. Creatinin per Kg. Body Weight	Convulsions
12-13	9,590	360	397.2 (computed)	41.4	Severe, frequent, generalized, lasting about one minute
13-14	.....	235	176.2	18.3	Generalized, repeated seven times, duration one-half to one minute
14-15	.....	270	116.0	12.2	No convulsions

TABLE 5.—*Creatinin Excretion of Case 2*

July	Weight	C.c. Urine	Mg. Total Creatinin	Mg. Creatinin per Kg. Body Weight	Convulsions
7-8	9,610	560	108.0	11.2	Three, slight, lasting one to one and one-half minutes, localized on face, right side
8-9	.....	757	104.5	10.8	One localized on face, right side

next two days, the urine collections were complete for each twenty-four hour period. His diet was whole milk, junket, custard and vegetables (785 calories), but the infant vomited large amounts of the food taken. His creatinin excretion is given in Table 4. One week later, convulsions were decreasing in frequency, duration and severity, but in view of their actual persistence in spite of large calcium intake and relatively normal blood calcium, 9.0 mg. per hundred cubic centimeters, the diagnosis of tetany became very doubtful and, although lumbar puncture showed no abnormality except a slight increase in spinal fluid pressure, some intracranial lesion was suspected.

In another case, we observed an infant having slight, localized convulsions, in whom creatinin excretion was normal.

CASE 2.—A. L., a well developed infant, aged 11 months, weighing 9.61 kg., was admitted to hospital on account of slight convulsions of unrecognized origin, occurring at times since the age of 6 months. The family history was suggestive of epilepsy. The infant was on the metabolism frame during 2 twenty-four hour periods. Urine collections were complete. The diet was milk, 35 ozs. His daily creatinin output may be seen in Table 5.

SUMMARY

The uric acid excretion per twenty-four hours was measured in a series of twenty-two male infants. The diet of the infants being purin free, the amounts of uric acid found are regarded as of endogenous origin. In contrast with most of the hitherto published measurements of uric acid in infants' urine, a closely constant daily excretion was found for the individual, and a fairly constant value per unit of body weight for the group of infants, the range being from 14 to 25 mg. of uric acid per kilogram of body weight.

Except in the case of an infant with active rickets whose uric acid excretion was high, 36 and 34 mg. per kilogram of body weight, no relationship of nutritional state to uric acid excretion was apparent. Uric acid excretion was also apparently independent of the age of the infant.

It is suggested that the relatively high level of excretion of endogenous uric acid by infants may be explained by their high protein intake; using the evidence obtained by Folin and his co-workers that a high intake of protein retards the destruction and accelerates the excretion of uric acid. It must be admitted, however, that in this series the relationship of urine nitrogen to uric acid was not close, uric acid nitrogen ranging from 1.25 to 3.5 per cent. of the total nitrogen.

Measurements of urine creatinin in the same group of infants support the conception of a close constancy of creatinin excretion in terms of the protoplasmic mass of the body. The range found was from 10 to 15 mg. per kilogram of body weight. The highest values were obtained in malnourished infants, probably because of their relatively larger mass of active tissue.

No relationship of creatinin excretion to differences in sleeping time or of muscular tonus was discernible. However, in the case of an infant having severe generalized convulsions, a creatinin excretion three to four times higher than normal was observed. Another infant with slight localized convulsions was found to excrete an approximately normal quantity of creatinin.

PLASMA CHLORIDES IN ACUTE INTESTINAL INTOXICATION OF CHILDREN *

GLADYS L. BOYD, B.S., M.D. (Tor.)
TORONTO, CANADA

In recent years much interest and varying degrees of importance have been attached to the chloride content of the blood plasma.[1] Hypochloremia has been noted in a number of such unrelated clinical conditions as severe superficial burns, pneumonia, war-gas poisoning, the pernicious vomiting of pregnancy and high intestinal obstruction.[2] Closer study reveals the fact that in spite of their diverse pathology, these conditions all have one of two factors in common. There is either a circulating toxin of a split protein nature as in intestinal obstruction [3] and burns,[4] or there is a rapid and severe loss of fluids as in war-gas poisoning, pernicious vomiting and pneumonia. In some instances there is a combination of the two. It was therefore thought that a study of the chlorides in acute intestinal intoxication in which fluid loss and a split protein intoxication [5] were both present would be of interest.

TECHNIC

On admission to the hospital during the past summer, samples of blood were obtained by puncture of the anterior fontanel in all patients with acute intestinal intoxication. The blood was transferred at once to graduated centrifuge tubes and centrifuged for one hour at 1,500 revolutions per minute. The serum was separated immediately and kept on ice when determinations could not be made at once.

The chlorides were determined by Rappleye's [6] method. In the tables their concentration is expressed as milligrams of sodium chloride in hundred cubic centimeters of plasma or serum, as the case may be. The normal values expressed this way vary from 570 to 650 mg. per hundred cubic centimeters of plasma. In this way, eighty-nine chloride

* Received for publication, Jan. 8, 1926.

* From the wards of the Hospital for Sick Children, and the research laboratories of the Sub-Department of Pediatrics, University of Toronto, under the direction of Alan Brown, M.B.

1. De Wesselow, O. L. V.: Internat. Clin. **3**:191 (Sept.) 1924.

2. Haden, R. L., and Orr, T. G.: Surg., Gynec. & Obst. **37**:465 (Oct.) 1923.

3. Whipple, G. H.: J. Exper. Med. **28**:213 (Aug.) 1918.

4. Robertson, B., and Boyd, G. L.: J. Lab. & Clin. Med. **9**:1 (Oct.) 1923.

5. Boyd, G. L.: The Etiology of Acute Intestinal Intoxication in Infants, Arch. Int. Med. **31**:297 (Feb.) 1923.

6. Rappleye, W. C.: J. Biol. Chem. **35**:509 (Sept.) 1918.

determinations were made in sixty-six cases, and the results may be classified as follows:

Thirty-three cases, normal; twenty-one cases, hypochloremia; twelve cases, hyperchloremia.

The disparity in these results and the fact that hypochloremia was found in less than half the cases was somewhat disconcerting. Perhaps the most obvious explanation would be afforded by differences in the degree of concentration, or dilution of the blood. To determine this factor, the cell volume, hemoglobin and plasma protein were estimated and the degree of dehydration clinically was noted. Not only did the laboratory and clinical criteria of anhydremia fail to coincide, but the

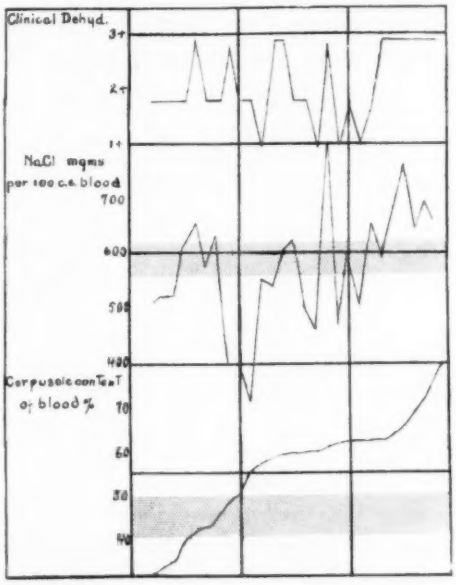


Chart 1.—The shaded areas indicate the normal range of plasma chloride and cell volume, respectively.

chemical evidences were so conflicting in themselves that we were forced to the conclusion that blood volume determinations were essential for any accurate data on this subject. The variations in the chloride content of the plasma in relation to the cell volume or clinical degree of dehydration are shown in chart 1. The relation noted between the plasma proteins and chlorides will be pointed out later. It has been claimed by certain observers, Adolph [7] and Marriott,[8] that the suddenness of the fluid loss was responsible for the effect produced by the dehydration

7. Adolph, E. F.: J. Physiol. **55**:114 (May) 1921.
8. Marriott, W. McK.: Physiol. Rev. **3**:275 (April) 1923.

on the chlorides, rapid loss being accompanied by hyperchloremia and gradual loss usually proving ineffectual. In fourteen of our patients in whom the rate of onset was accurately observed, this held true. In seven with sudden overwhelming toxemia, the average chlorides were 677 mg. per hundred cubic centimeters of plasma, while in those of insidious onset the average obtained was 590 mg. per hundred cubic centimeters.

Secondly, was the toxemia itself responsible for the depression of the chlorides, as in intestinal obstruction,[9] and was the degree of hypochloremia of some prognostic value? The degree of toxemia depending entirely on clinical observation must be merely relative.

The lack of any close relationship between the chlorides and the degree of toxemia is apparent from the table. It might be stated that all extremely low chlorides were found in severely toxic cases; their lack of prognostic import, however, may be gathered from the fact

Amount of Chlorides in Toxemia *

Plasma Chlorides	Number of Cases	Degree of Toxemia		
		1	2	3
Normal	18	5	4	9
High	7	2	1	4
Low	12	4	5	..

* The degree of toxemia present is indicated by the numerals 1, 2 and 3, 1 representing a mild toxemia and 3 a severe one.

that the chlorides in the fatal cases varied from 450 to 900 mg. per hundred cubic centimeters of plasma.

Fever is at once a variable factor in acute intestinal intoxication, and according to McLean [10] a potent cause of reduction of the plasma chlorides. The temperature in this series of cases varied widely, in some instances due to intercurrent infections, in others inexplicable unless by the dehydration present. The cause of the pyrexia appeared of little moment in this regard, and no uniformly low chloride figures were obtained in the fevered, the temperature in cases of hypochloremia varying from 97 to 103 F.

SUGAR DETERMINATIONS

Sugar determinations were made on all samples of blood taken, because of the abnormalities recently noted in the carbohydrate metabolism in this condition by Tisdall [11] and his co-workers. No uniformity

9. Haden, R. L., and Orr, T. G.: J. Exper. Med. **38**:55 (July) 1923.
10. McLean, F. C.: J. Exper. Med. **22**:212, 1915.
11. Tisdall, F.; Drake, T., and Brown, A.: J. Lab. & Clin. Med. **9**:458.

was obtained in the results. It is not the intention here to discuss these results except so far as they bear a possible relationship to the chlorides. Herrick [12] recently pointed out a reciprocal relationship between these two crystalloids of the blood. Chart 2 illustrates the findings in our cases, and demonstrates a fairly close agreement with Herrick's observation on his office patients. The only exceptions to the general rule were two patients in whom low chlorides and low sugars were present. They may be regarded as due to blood dilution, as cell volumes were 33 and 36 per cent, and hemoglobin 55 and 60 per cent, respectively.

This relationship between the chlorides and sugars of the blood could be explained on the basis of the maintenance of the osmotic pressure,

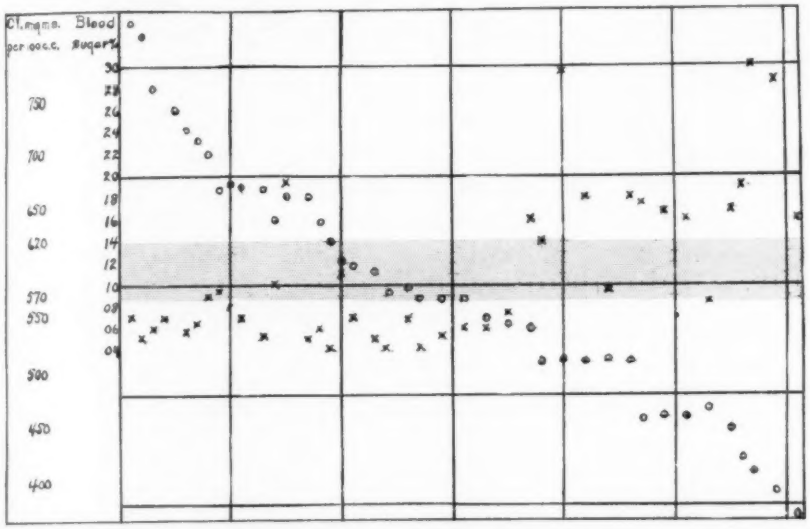


Chart 2.—In chart 2, 0 indicates milligrams of chloride as sodium chloride, and x the percentage of sugar in the blood. The shaded area represents the normal range of these values.

or acid base equilibrium of the blood. It was thought that the comparisons of the chlorides and proteins of the blood might help in the elucidation of this problem. The latter were estimated by the refractometer routinely as checks on the concentration of the blood, but as mentioned previously failed to be of use for this purpose. Chart 3 indicates an even more consistent reciprocal relationship between the proteins and chlorides of the plasma, than shown between the latter and the blood sugar. The only exceptions noted are indicated in chart 3, and occurred in those cases in which the high protein of the serum was associated with evidences of anhydremia.

12. Herrick, W. W.: J. Lab. & Clin. Med. **9**:458.

SUMMARY AND CONCLUSIONS

The plasma chlorides were studied in sixty-six cases of acute intestinal intoxication in infants. Hypochloremia, anticipated because of its association with other toxemias of similar nature, was found in less than one-half of the cases studied. Varying degrees of blood dilution were at first considered as being responsible for the wide variations in chloride content found, but although we were early forced to the conclusion that cell volume, hemoglobin and protein concentration furnished inadequate estimates of this condition, such evidence as we had rendered this explanation unlikely. Blood volume determinations will be indispensable in ascertaining whether blood dilution is a factor in causing the wide fluctuations in the plasma chlorides found.

The second, and perhaps the most plausible theory to some, to account for the results obtained would be the severity of the toxemia.

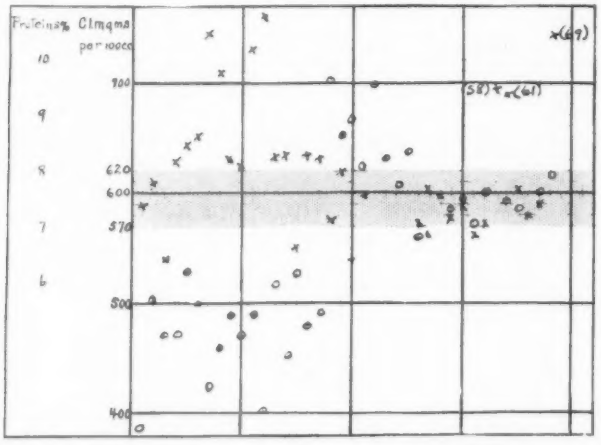


Chart 3.—In chart 3, 0 indicates milligrams of chloride as sodium chloride in hundred cubic centimeters; x indicates the percentage of protein in the same cases. The figures before x indicate the cell volume in these cases, which were exceptional, as the high protein content was associated with normal chloride. The darkened area indicates the normal range.

Clinical estimations of the latter are necessarily crude, but are the only ones available. No definite relationship between the chloride concentration and the toxemia present can be demonstrated. Extremely low chlorides were found only in severely toxic subjects, but not all those severely toxic had low chlorides, and even in fatal cases normal or high chlorides were found. It is quite obvious that the blood chlorides are of no prognostic importance.

No correlation was observed between the plasma chlorides and any other symptoms or signs of the disease. Fever had no effect whatever. Severe diarrhea was present in 84 per cent of those having low

chlorides, but all severe diarrheas were not accompanied by hypochloremia. Accurate estimations of the amount of vomitus were not made, but in no subject with low chlorides did the vomiting appear sufficiently severe clinically to have been the cause of their reduction.

An interesting reciprocal relationship was noted between chlorides and proteins, and chlorides and sugar. Theories to account for these phenomena are purely speculative without further work. The chloride-protein relationship would appear to be an expression of the disturbed acid base equilibrium which is present in this disease. McLean [13] has pointed out the linear relationship between the hydrogen ion concentration and the proteins of the blood, and mentions the tendency to decreased chloride concentration when the proteins are high. Conjecture regarding the chloride-sugar relationship is beset with even greater difficulties, as both acid base relationship and carbohydrate metabolism are involved. Allen [14] has shown that depletion of carbohydrate, such as would be produced by their defective utilization recently reported by Tisdall in this type of intoxication, produces an acidosis. It would seem as likely that the reciprocal relationship shown between chlorides and sugars would be due to the disturbed acid base relationship present. The coincident determination of the hydrogen ion concentration, plasma bicarbonate, proteins, sugars and chlorides will be necessary to clear up this problem.

---

13. McLean, F. C.: Physiol. Rev. **5**:625.
14. Allen, F. M.: J. Metabol. Res. **4**:199 (Oct.) 1925.

A QUANTITATIVE METHOD FOR THE DETERMINATION OF THE COMBINED UREA AND AMMONIA NITROGEN OF SALIVA*

FREDERIC W. SCHLUTZ, M.D.
AND
MILDRED R. ZIEGLER, M.S.
MINNEAPOLIS

Quantitative studies of salivary constituents were seldom, if ever, undertaken five years ago. This was due to the cumbersome methods then in vogue. With the application to saliva of the rapid and accurate microchemical methods of blood analysis, more attention has been directed toward the salivary constituents, and especially toward urea, as a diagnostic aid.

After the discovery of urea in saliva by Pettenkoffer and Wright,[1] Picard, Poisseuille, Bechamp and Gréhant [1] made a few isolated determinations. Their results were varied, probably on account of the necessity of using the old hypobromite method. The first accurate quantitative studies of urea, made by Hench and Aldrich [2] and by Schmitz,[3] were followed by those included in the extensive researches of Updegraff and Lewis,[4] and Morris and Jersey.[5] These authors have shown that the combined urea and ammonia nitrogen content of saliva closely parallels that of blood urea nitrogen.

The method published herewith was worked out over a year ago, and proved satisfactory at the pediatric clinic of the University of Minnesota. It is valuable because of the ease of collecting saliva compared with the difficulty of obtaining blood. This method is a modification of that for the determination of blood urea, described in Folin's "Laboratory Manual of Biological Chemistry." The values obtained by its use approximate those of blood urea nitrogen more closely than do the results afforded by any other published method. The saliva is collected without the use of a stimulant, as Morris and Jersey [5] have shown that the secretion is less subject to irregularities in chemical content when thus procured. The determinations are made immediately after collection. It is most probable that the nitrogen fraction obtained by this

* Received for publication, Oct. 18, 1925.

* From the Department of Pediatrics, Medical School, University of Minnesota.

1. Pettenkoffer and Wright; Picard, Poisseuille, Bechamp and Gréhant, quoted by Schöndorff, B.: Arch. f. d. ges. Physiol. **74**:318, 1899.

2. Hench, P. S., and Aldrich, M.: The Concentration of Urea in Saliva, J. A. M. A. **79**:1409, 1922.

3. Schmitz, H. W.: J. Lab. & Clin. Med. **8**:78 (Nov.) 1922.

4. Updegraff, H., and Lewis, H. B.: J. Biol. Chem. **61**:633 (Oct.) 1924.

5. Morris, J. L., and Jersey, V.: J. Biol. Chem. **56**:31 (May) 1923.

method is all, or at least largely, urea nitrogen, as the ammonia content is extremely variable and increases rapidly on standing, probably from bacterial decomposition.

METHOD

Ten cubic centimeters of saliva collected without the use of a stimulant is immediately shaken for five minutes with 2 gm. of nitrogen-free kaolin and filtered. The kaolin is prepared in quantity from Merck's kaolin by washing twice with 2 per cent. acetic acid, four or five times with distilled water, filtering and drying. If the filtrate is turbid, the process is repeated. To 1 c.c. of the saliva filtrate in a 75 c.c. pyrex test tube add 4 c.c. of distilled water, 2 drops of Folin's pyrophosphate buffer mixture and 1 c.c. of his urease solution. This is heated in a water bath, from 40 to 55 C., for five minutes. The ammonia, including

Experimental Results

	Urea N. in Blood Mg. per 100 C.c.	Urea N. in Saliva Mg. per 100 C.c.
Normal Subjects:		
W. W. S.	13	12*
	13	12*
M. M.	15	10*
	16	13*
F. W. S.	12	13
L. F. R.	15	15
W. W. S.	12	13
M. M.	13	12
H.	16	16
M.	14	14
S.	8	7
Hospital Subjects:		
A. W., Nephrosis and edema	15	16
L. A., Nephritis	42	27*
L. P., Prostatic obstruction	91	96
H. U., Prostatic obstruction	114	112
B. E., Prostatic obstruction	141	118
R. J., Nephritis	52	46

* Saliva collected by paraffin stimulation.

that formed from the urea, is removed by aeration after the addition to the digestion mixture of a little liquid petrolatum and 2 c.c. of 10 per cent. sodium hydroxide. It is collected in a test tube graduated at 25 c.c. and containing 2 c.c. of 0.05 normal hydrochloric acid diluted with about 10 c.c. of water. After fifteen minutes aeration, dilute the contents of the receiver to 20 c.c., add 2.5 c.c. of Nessler's solution, make up to 25 c.c., and compare in the colorimeter with a standard containing 0.3 mg. of nitrogen (in the form of ammonium sulphate) and 10 c.c. of Nessler's solution in a 100 c.c. flask.

Calculation:

$$\frac{\text{Reading of standard in mm.}}{\text{Reading of unknown in mm.}} \times 0.3 \times \frac{1}{4} \times \frac{100}{1} = \text{mg. of ammonia and urea N. per 100 c.c. of saliva}$$

Samples of blood and saliva were collected simultaneously. The determination of blood urea nitrogen was carried out according to the directions of Folin and Wu, using the aeration method.

PARATYPHOID FEVER

REPORT OF A CASE IN AN INFANT*

DAVID GINGOLD, M.D.
AND
HARRY WEXLER, M.D.
BROOKLYN, N. Y.

Previous History.—S. G., a boy, aged 18 months, was born at term, of normal delivery, the birth weight being 8 pounds (3,808 gm.). He was breast fed for eight months. Gradually thereafter, cows' milk, boiled, cereals, stewed fruits, vegetables and egg were added. The child sat up at 7 months and began to walk at the age of 13 months. The weight at 1 year was 22 pounds.

Present Illness.—For the past three months, the patient suffered with severe abdominal pain; he would suddenly scream, point to the abdomen, and draw up his knees. Several such attacks occurred daily. About four weeks prior to admission to the hospital, the mother noticed a progressive pallor and some loss of weight. At about the same time, a bowel movement occurred in which blood was noted.

On Feb. 7, 1925, the baby was admitted to the Babies Hospital, New York City. In a communication from that institution, the following is noted: "Chief complaint, extreme pallor and attacks of abdominal pain; red blood corpuscles, 3,568,000; blood platelets, 296,000; white blood corpuscles, 10,600; polymorphonuclears, 71 per cent.; lymphocytes, 25 per cent.; mononuclears, 3 per cent.; transitionals, 1 per cent; nucleated cells, 17 per cent.; the Wassermann blood test was negative; the stools show no parasites or ova. Diagnosis: secondary anemia, unimproved." The child was discharged on February 13, on request of the parents. During his stay at the Babies Hospital the temperature was normal.

On February 17, Dr. Gingold saw the baby in consultation, and the patient was admitted to the Beth Moses Hospital the same day, with a temperature of 103.4 F.

Physical Examination.—The child was fairly well developed, about 18 months of age, very pale, and appeared quite ill. The mucous membrane of the mouth was pale. The anterior fontanel was almost completely closed. The chest findings were negative. On examination of the heart, a systolic mumur, soft and blowing in character and not transmitted, was heard best at the apex. The abdomen was soft and slightly distended. The liver was enlarged to about 6 cm. below the costal margin. The spleen was not palpable. Over the epigastrium and right hypochondrium, tenderness to superficial and deep palpation was present. Slight edema of both ankles was present. The inguinal and axillary lymph nodes were moderately enlarged. No meningeal signs were present.

Laboratory Examinations.—Hemoglobin, 45 per cent. (Sahli); red blood cells, 3,300,000; leukocyte count, 13,000; differential polymorphonuclears, 70 per cent.; eosinophils, 1 per cent.; basophils, 2 per cent.; lymphocytes, 27 per cent. Examination of a blood smear (Wright's stain) revealed no abnormal white blood cells. The red blood cells showed the presence of occasional macrocytes and microcytes. Polychromatophilia and poikilocytosis were present. No stippling or myeloblasts were seen. Blood platelets, 192,000 per cubic millimeter. Bleeding time, 1.75 minutes; coagulation time, 4.25 minutes. Fragility Test:

---

* Received for publication, Nov. 10, 1925.

* From the Department of Pediatrics, Beth Moses Hospital.

Initial hemolysis at 0.40 per cent., complete at 0.28 per cent. Stool examination: blood present (Benzidine). No ova or parasites were seen. The Mantoux test was negative.

On February 22, a blood culture was reported as positive for *Bacillus paratyphosus* B. Blood serum agglutination was positive for *Bacillus paratyphosus* B, in dilutions 1:40, 1:80 and 1:160. Culture of urine and stools on several occasions were negative for *Bacillus paratyphosus* B.

Clinical Course.—On February 22, owing to the marked secondary anemia, the patient was given a transfusion of 250 c.c. of citrated whole blood by the direct method. A few days following admission, a few suspicious, scattered "rose spots" were noted on the lower part of the abdomen and on the thighs. Several similar "rose spots" made their appearance on successive days.

The child was placed on a diet of lactose, fruit juices, buttermilk and strained gruels. The temperature began to subside gradually and became normal within ten days after admission to the hospital. The appetite began to improve, the patient became interested in his surroundings, and he ceased to complain of abdominal pain. At no time during his stay at the hospital was any diarrhea present. The spleen was never found to be enlarged. Repeated blood examinations were made. The hemoglobin rose gradually and the red blood cells increased in number. On the day of discharge, April 9, the hemoglobin was 75 per cent. (Sahli), the red blood cells 4,280,000, there being no atypical forms present.

COMMENT

We are not prepared to state with certainty that the infection by the *Bacillus paratyphosus* B was of several months' duration. This is somewhat difficult to conceive, particularly in view of the rather long afebrile period. However, the severe abdominal pain coupled with the marked secondary anemia, which, in all probability, was due to repeated small hemorrhages from the bowel, may have been due to a low grade type of infection of which the *Bacillus paratyphosus* B was the causative agent.

It is rather surprising to note that comparatively little or no mention is made of paratyphoid fever in the standard pediatric textbooks. That paratyphoid fever in children is not so rare as the current literature and textbooks would suggest, is indicated by Stolkind and Lorey.[1] These authors classified cases reported by them as (1) typhoid form, (2) gastro-intestinal form, (3) choleraic form, (4) respiratory or influenzal form. The majority of the patients presented diarrhea, bronchitis and fever; with temperature curves ranging from 99 to 105 F. Fifty per cent. had enlarged spleens. Invariably, *Bacillus paratyphosus* B was recovered from the blood or the stools. The prognosis was usually good, and the mortality ranged from 0 to 3 per cent., depending on complications.

That meningeal signs may be present in paratyphoid fever in children, is described by Lehmann.[2] In a series of sixteen patients, with

1. Stolkind, E., and Lorey, A.: Paratyphoid Fever in Children, Brit. J. Child. Dis. **15**:161 (July-Sept.) 1918.

2. Lehmann, F. R.: Über den Klischen verlauf von sixteen Paratyphus B Fällen im Saüglings und Kleinkinesalter, Deutsch. med. Wchnschr. **50**:575 (May) 1924.

ages ranging from 2 to 21 months, a considerable portion exhibited meningeal signs with bulging fontanel, rigid neck and opisthotonus. The spinal fluid was usually normal. In fourteen cases, *Bacillus paratyphosus* B was isolated from the blood.

Severe abdominal pain, as manifested by the drawing up of the knees, occurred in a case reported by Wisch.[3] This was an infant, a girl, aged 5 months, with persistent fever, vomiting, and from eight to ten bloodstained stools daily. The stool culture was positive for *Bacillus paratyphosus* B. The blood serum agglutinated *Bacillus paratyphosus* B in 1 : 80 dilutions.

General abdominal pain, which was so conspicuous in the case reported by us, was found to be present in about one-half of the cases of paratyphoid fever in cases reported by Knox.[4]

That a surgical condition may complicate an infection by *Bacillus paratyphosus* B is shown by Wordley.[5] A boy, aged 4, with a previous history of diarrhea, developed an effusion into the right shoulder joint. Aspiration of the fluid, followed by culture, revealed *Bacillus paratyphosus* B.

Mendelssohn[6] warns against overlooking a *Paratyphosus* B infection in infants with continuous fever and alimentary symptoms, particularly with associated meningeal signs which cannot be attributed to any of the other infectious agents.

In cases observed by Achard and Thiers,[7] it was noted that (1) diarrhea was usually prolonged, (2) "rose spots" were of inconstant occurrence, (3) fever might be of moderate degree and (4) the usual duration of the disease varied from fifteen to twenty-five days.

SUMMARY

A case of paratyphoid fever in an infant, aged 18 months, is reported. The salient clinical features were persistent abdominal pain of three months' duration, marked secondary anemia, a relatively brief febrile period, and isolation from the blood of *Bacillus paratyphosus* B.

3. Wisch, Louis J.: Paratyphoid Fever in a Baby, J. Indiana M. A. **16**:204 (June) 1923.

4. Knox, J. H. Mason, Jr.: Paratyphoid Fever, Abt's Pediatrics **6**:32, 1925.

5. Wordley, F.: Unusual Case of Paratyphoid Infection, Lancet **2**:794 (Oct. 16) 1920.

6. Mendelssohn, A.: Über Paratyphus im Saüglings alter, Monatschr. f. Kinderh. **28**:348 (July) 1924.

7. Achard, C., and Thiers, J.: Fièvre Paratyphoide B chez un nourrisson, Bull. de l'Acad. de mèd., Paris **91**:218 (Feb. 12) 1924.

PROGRESS IN PEDIATRICS

APPENDICITIS IN CHILDREN UNDER FIVE YEARS OF AGE *

FREDERICK CHRISTOPHER, M.D.
Junior Surgeon, Evanston Hospital; Associate in Surgery, University of Illinois Medical School
WINNETKA, ILL.

Acute appendicitis in children under 5 years of age is a relatively infrequent disease. Even in the surgical services of large hospitals there is but small opportunity to see many cases. A study of this subject, therefore, must involve a careful examination of the literature. A collective consideration of the reported cases and statistics should give information which the experience of the isolated writer generally is unable to furnish.

Contributions to this subject have been made by pediatricians and by surgeons. Numerous inaugural dissertations have made it their theme. Some writers have been able to present a very considerable series of cases, and individual case reports have also been numerous.

The following paper is, first, an effort to make a critical examination of the present knowledge of the subject; second, to present several illustrative cases, and third, to draw certain conclusions which seem to have outstanding importance.

The incidence of appendicitis under the age of 5 years may be estimated from statistics of hospital admissions and from mortality statistics.

HOSPITAL AND MORTALITY STATISTICS

In the Liverpool Infirmary for Children,[1] no cases of perityphilitis, pericolitis, or appendicitis were mentioned in the statistics of the years from 1876 to 1891. Yet there were some 14,000 new cases per annum in this institution. From 1911 to 1913 the death rate from appendicitis in children under 5 years in England and Wales was 60 per 1,000,000 population.[2] The mortality from appendicitis in England and Wales in 1918 was almost double that of 1901, a circumstance which may probably be attributed to the faulty recognition of the earlier cases.[3] At present, appendicitis is felt to be by far the commonest surgical disease

* Received for publication, Feb. 24, 1926.

1. Simpson, G. C. E.: Brit. J. Child. Dis. **10**:400, 1913.
2. Stoumann: Am. J. Pub. Health, **6**:714 (July) 1916.
3. Brown, H. H., and Cade, H. M.: Lancet **1**:118 (Jan. 15) 1925.

of young children.[4] Sixty per cent of all laparotomies in children are for this disease,[5] and it is thought that the appendix is the cause of 95 per cent of the cases of peritonitis in children (footnote 4, second reference). Of 100 consecutive laparotomies at the Children's Hospital, Dublin,[6] thirty-seven were for acute and chronic appendicitis, nineteen for tuberculous peritonitis, and seventeen for intussusception. In the last five years at the Evanston Hospital, there were eighteen cases of acute appendicitis in children 5 years and under to six cases of intussusception. For children aged 3, or under, in this time there were eight cases of appendicitis to six of intussusception.

This importance of appendicitis as a cause of death, compared to certain other diseases in the first 5 years of life, may be judged from table 1, compiled from the United States Statistics [7] for 1922.

TABLE 1.—*Number of Deaths Registered in the United States in 1922*

Cause of Death	Number of Deaths in the Registration Area of U. S., Exclusive of Hawaii, in 1922
Appendicitis and typhilitis	516
Meningococcus meningitis	477
Nonepidemic cerebrospinal meningitis	466
Tetanus	452
Acute anterior poliomyelitis	428
Rickets	409
Diseases of kidneys and adnexa	342
Cancer	302
Tuberculosis of intestines and peritoneum	292
Encephalitis	254
Epilepsy	210
Diabetes mellitus	202
Chronic nephritis	176
Hernia	174
Lethargic encephalitis	164
Smallpox	82

During this time (1922), the mortality from intestinal obstruction in the first 5 years of life was 1,485; first year, 1,051; second, 195; third, 103; fourth, sixty-six; fifth, seventy. It is not improbable that a certain number of these deaths could be attributed to peritonitis of appendiceal origin.

Another method of estimating the importance of appendicitis in the first 5 years of life is the fact that 4 per cent of all deaths from appendicitis occur in these years. This will be apparent from consulting table 2.

In the Registration Area of the United States, exclusive of Hawaii, in 1922 there were 1,101,863 deaths. The deaths in the first 5 years numbered 218,201. The percentage of deaths from appendicitis of all ages of the number of deaths from all causes of all ages was 1.2. The

4. Green, S. F. St. D.: Practioner **89**:508, 1912. Stuot, M. E.: J. Oklahoma M. A. **16**:11 (Jan.) 1923; Bolling, R. W.: J. A. M. A. **83**:963 (Sept. 27) 1924.

5. Vincent, Beth: Boston M. & S. J. **159**:427 (June) 1908.

6. Barrett, J. B.: M. Press & Circular **99**:392, 1915.

7. Mortality Statistics, 1922, Bureau of Census, Washington, D. C.

percentage of deaths from appendicitis under 5 years of the number of deaths from all causes under 5 years was 0.2.

Whereas the first 5 years of life account for 4 per cent of the deaths from appendicitis, only 2 per cent of all cases of appendicitis occur in these years. This figure is suggested by table 3.

In 1908, Deiss [8] found that for 899 admissions to a children's hospital, aged from 0 to 6 months, there was one case of appendicitis; from 6 to 12 months, 466 admissions with one case; from 1 to 3 years, 1,570 admissions with twelve cases; from 3 to 5 years, 1,090 admissions with

TABLE 2.—*Mortality Statistics: Deaths from Appendicitis and Typhilitis*

Place	Year	Under 1 Year	1 Year	2 Years	3 Years	4 Years	Total Deaths Under 5 Years	Total Deaths Appendicitis All Ages	Per Cent Under 5 Years
U. S. registration area exclusive of Hawaii	1922	50	56	114	144	152	516	13,229	3.9
State of Illinois.....	1923	2	2	11	21	17	53	1,146	4.5
State of Illinois.....	1924	10	9	11	23	12	65	1,100	5.9
Total.....		62	67	136	188	181	634	15,475	4.0

TABLE 3.—*Appendicitis in 5 Years and Under as Compared with Appendicitis of All Ages*

Author and Hospital	Date of Report	Total Cases Collected	Number 5 Years and Under	Per Cent 5 Years and Under
McCosh (J. A. M. A. [Sept. 24] 1904).....	1904	1,000	17	1.7
Churchman, Johns Hopkins Hospital.....	1909	1,223	9	0.73
Steven, London Hospital (Practitioner **89**: 527, 1912)	1912	4,000	80	2.0
Maylard (Brit. J. Surg. **8**: 189, 1920).....	1920	1,000	4	0.4
Flint (Practitioner **104**: 352, 1920).....	1920	370	5	1.38
Suermondt (Deutsche Ztschr. f. Chir. **170**: 289, 1922)	1922	1,000	2	0.2
Marsch (Beitr. z. klin. Chir. **126**: 67, 1922).....	1922	4,000	44	1.1
Bolling, St. Luke's Hospital, New York.....	1924	888	31	3.5
Christopher, Evanston Hospital, Evanston, Ill.....	1926	533	18	3.37
Total.....		14,014	210	1.49
Kelley, collected from twenty-two authors (Ill. M. J. **43**: 454, 1923)	1923	16,571	400	2.41

eleven cases; from 5 to 10 years, 1,593 admissions with forty-two cases. From 3 to 5 years 1.01 per cent of the admissions were for appendicitis, while from 5 to 10 years, the percentage was 2.63. There was a preponderance of cases in the male, an observation which is shared by other observers.

ETIOLOGY

While it is becoming more evident that appendicitis in infants is not as rare as one might believe,[9] little can be said with surety as to the etiology. In 1912, Cecil and Bulkley [10] found 15 per cent of 129 cases

8. Deiss, Franz: Inaugural Dissertation, Basel, 1908.
9. Kamenetzky, Zachary: L'Appendicite chez l'enfant, Thèse, Lyon, 1914.
10. Cecil and Bulkley: Am. J. M. Sc. **143**:193, 1912.

of appendicitis in children to be caused by *Oxyuris vermicularis* or by *Trichocephalus trichiura.* One writer (Marsch) even goes so far as to say that in about 50 to 60 per cent of all cases with the picture of appendicitis, oxyuris may be found in the appendix. Rheindorf [11] found oxyuris in six of thirteen children, aged from 3 to 12 years, who died of appendicitis. In 1909, Farssac [12] emphasized what he believed to be "indisputable relationship of cause and effect between affections of the nasopharynx and the appendix." He believed that appendicitis of nasopharyngeal origin always occurred after an acute attack involving the tonsils and adenoids, the infection being transmitted by the digestive tract or by the blood stream. Infants are especially menaced by this complication of acute and chronic affections of the pharynx. Foreign bodies and fecoliths play a negligible etiologic rôle. Infectious diseases, familial predisposition, and mechanical causes have been thought to have an etiologic rôle.[13] Abt [14] believes that traumatism or diseases of the alimentary tract play a part in the causation of appendicitis. One should watch for appendicitis during and immediately after tonsillitis and the acute exanthemas, especially measles.[15]

A transient vermiform appendix is said to be present at the seventh to eighth week in utero.[16] Later, the primary differentiation of the appendix comes as a narrowing of the distal portion of the cecum, and at birth a secondary differentiation with the development of sacculation of the large intestine occurs.

As Ricketts [17] remarked, "an infant at the time of birth may have an appendix as large in every particular as a giant." The ratio of the length of the appendix to the length of the alimentary canal is as 1 is to 71 in the new-born, and as 1 is to 115 in the adult (Meckel). The ratio of the length of the appendix to the length of the large intestine is as 1 is to 10 in the new-born and as 1 is to 20 in the adult (Ribbert). Ribbert is quoted by Yoshida [18] as giving the average length of the appendix at birth as 5.7 cm., and by Piersol [19] and by Eitel [20] as 3.4 cm. The average length up to 5 years is 7.6 cm.; from 5 to 10 years, 9 cm.;

---

11. Rheindorf, quoted by Richter: Berl. Klin. Wchnschr. **10**:451, **11**:503, 1912.
12. Farssac, R. C. F. M.: Thèse, Bordeaux, 1909.
13. Kee, A. L.: West. M. Rev., Omaha **17**:125, 1912.
14. Abt, Isaac A.: Arch. Pediat. **34**:459 (Sept.) 1917.
15. Peple, W. L.: Old Dominion J. Med. & Surg. **20**:175, 1915-1916.
16. Kelly, H. A., and Hurdon, E.: The Vermiform Appendix, Philadelphia, W. B. Saunders Company, 1905.
17. Ricketts, B. M.: The Appendix Vermiformis and Cecum, J. A. M. A. **36**:1536 (June 1) 1901.
18. Yoshida, Tanzo: Inaugural Dissertation, München, 1908.
19. Piersol: Human Anatomy, Philadelphia, W. B. Lippincott, 1907, p. 1665.
20. Eitel, G. G.: The Processus Vermiformis, J. A. M. A. **33**:263 (July 29) 1899.

from 10 to 20 years, 9.7 cm.; from 20 to 30 years, 9.5 cm.; from 30 to 40 years, 8.7 cm.; from 40 to 60 years, 8.5 cm.

In the infant, the entire ileocecal apparatus is at a somewhat higher level than McBurney's point,[16] and in fact the cecum is often above the anterior superior spine of the ilium.[19] Gundobin [21] notes that in 6 per cent of infants the appendix descends into the small pelvis, and in 22 per cent it lies posterior to the cecum. Schellong [22] reports a case of left-sided appendicitis following varicella in a constipated infant, aged 1¾ years. In the early years of life, there is a larger communication between the cecum and the appendix, a circumstance which doubtless hinders fecal stoppage.[23] The abundance of lymphoid material in the appendix of the child is thought by some [5] to account for the rapidity of the progress of the disease at that age. Lewis [24] has noted that the intestinal walls of the new-born seem to be permeable to bacteria which those of older infants, children, and adults do not permit to pass. The early development of gangrene is characteristic of appendicitis in young children. In the infant, the omentum has been but a relatively impotent factor as a protection against the spread of abdominal inflammation,[25] which circumstance is probably due to its small size. While most writers feel that the appendix is a vestigial structure, Barry [26] of Edinburgh feels that it is a specialized part of the alimentary canal. Koga [27] recalls the interesting observation of Lucas-Championiere that among 22,000 Roumanian peasant patients who lived almost exclusively on a vegetarian diet, there was but one case of appendicitis. In German cities there was one case of appendicitis to every 221 patients hospitalized.

EARLY APPEARANCE OF APPENDICITIS

Perhaps the earliest case of appendicitis in the very young was that of a boy, aged 5 years, reported in 1812 by Parkinson.[28] In 1870, Betz published a paper entitled," Ileus in a Child Seven Months Old, Resulting from Perforation of the Appendix and Agglutination of the intestines." Jackson's case [29] is generally referred to in the literature on this subject. In this case, death was caused by bichloride of mercury poisoning forty hours after birth. At necropsy, an elongated and con-

21. Gundobin, quoted by Abt: Besonderheiten des Kindesälter, 1912.
22. Schellong, O.: Med. Klin. **4**:1722, 1908.
23. Seifert, E., and Augustin, E.: Arch. f. klin. Chir. **120**:35, 1922.
24. Lewis, Dean: Abt's System of Pediatrics **6**:625.
25. Speed, K.: Am. J. Surg. **37**:97 (May) 1923.
26. Barry: J. Anat. & Physiol. **35**:15-83, 1901. Quoted by Green, S. F. St. D.: Practitioner **89**:508, 1912.
27. Koga, Eishin: Inaugural Dissertation, München, 1910.
28. Parkinson, quoted by Kelly and Hurdon: The Vermiform Appendix.
29. Jackson, W. F.: Am. J. M. Sc. **127**:710, 1904.

gested appendix bound down by adhesions was found. The most conclusive case of prenatal appendicitis is that of Hill and Mason.[30] On delivery, the child's abdomen was markedly distended. Vomiting occurred on the first day, although the temperature was normal and meconium passed freely. On the second day the distention was extreme, the vomiting continued and the temperature was 102 F. The child died on the third day, fifty-five hours after birth. Necropsy disclosed that the peritoneal cavity contained 1,300 cc. of straw-colored clear fluid. The peritoneum was injected to a bright pink. The intestines were matted together with many fibrinous adhesions. The terminal ileum and cecum were darkened and swollen. The appendix, which was dark and swollen, was 2 inches long. There was a perforation in it one-fourth inch from the cecum. The appendix was filled with pus and débris. The fluid from the peritoneal cavity showed no organisms in smears, and failed to produce any growth when planted on various mediums.

Mention must be made of Griffith's [31] important paper in 1901, which was virtually a pioneer in this field. He reported a case of appendicitis in a child, aged 3 months.

In 1917, Abt [14] reported an infant, aged 9 months, who died of appendicitis without an operation; in addition he presented a critical review of seventy-nine other cases collected from the literature. There were twenty subjects under 3 months of age, of which sixteen were males and four females. Ten died and ten recovered. Eight of the twenty were associated with strangulated hernia. Convulsions occurred in none of these cases under 3 months, and in no instance was there any foreign body found in the appendix. In eight cases the appendix was gangrenous, and in seven perforated. In Abt's second group, that is, in children from 3 to 6 months of age, there were six subjects, of which four were males and two were females. Three died and three recovered. In two cases there were fecal concretions in the appendix. In the group aged from 6 to 12 months, there were eleven cases, of which seven were males and two were females, and in two cases the sex was not given. Seven died, three recovered and the fate of one is not recorded. Only two cases were associated with strangulated hernia. In two cases, fecal concretions are reported. In the fourth group, infants aged from 1 to 2 years, there were forty cases, of which twenty-five were males, eight females, and in seven the sex was not given. In four of these subjects, the appendicitis was complicated by a strangulated hernia. There were sixteen deaths, eighteen recoveries and in six cases the result was not recorded.

---

30. Hill, W. B., and Mason, C. C.: Prenatal Appendicitis with Rupture and Death, Am. J. Dis. Child. **29**:86 (Jan.) 1925.

31. Griffith, J. P. C.: Univ. Penn. M. Bull. **14**:300, 1901.

In addition to Abt's cases may be mentioned those of (*a*) Lannay [32] of acute appendicitis in a hernial sac in an infant, aged 28 days; (*b*) of Gloniger,[33] of successful operation for an inflamed appendix in an infant forty-one hours old, in which part of the small intestine, the cecum and the transverse colon were in the proximal umbilical cord, and of (*c*) Buford,[34] of an 8 months' old baby with intussusception and a gangrenous appendix. Vargas [35] describes a case of "agenesia cutanea perumbilical" with prolapse of part of the intestines. Appendectomy was performed twelve hours after birth and the baby recovered.

Reed's [36] case is a curiosity worthy of special mention. Reed was called to deliver a Mexican woman living in a dirty hovel. The baby was born with the entire large and small intestine outside of the abdomen. The intestines were sprinkled with straw, feathers, crumbs of food, and fecal matter. Circumstances made it necessary to leave the baby in this condition wrapped in a blanket. Two hours later, the baby was placed on the operating table. The intestines were cleaned off as well as possible. The appendix which was red, contused and swollen, was removed. The umbilicus was enlarged and the intestines were replaced. The child recovered!

DIAGNOSIS OF ACUTE APPENDICITIS

The diagnosis of acute appendicitis in children under 5 is generally agreed to be difficult, although to a few men the task seems easy [37] The present status of our ability to make a diagnosis in young children has been likened to our ability to make the diagnosis among adults twenty years ago.[38] Finney [39] has said that "in the adults, the tendency is perhaps rather to mistake something else for appendicitis, while in the child it is to mistake appendicitis for something else." Every acute abdominal condition in childhood should be considered as appendicitis until it has been proved otherwise, according to Helmholz [40] and likewise Deaver.[41] Two special peculiarities have been noted of appendicitis in childhood,[39] (1) the insidiousness of the onset, and (2) the rapidity of the progress to gangrene and perforation.

---

32. Lannay: Bull et mém. Soc. de Chir. de Paris **34**:680, 1908.
33. Gloniger, quoted by Kelly and Hurdon.
34. Buford, R. K.: Report of Case of Intussusception with Gangrenous Appendix, J. A. M. A. **74**:460 (Feb. 14) 1920.
35. Vargas, M.: Siglo Med. **64**:870 (Nov. 17) 1917.
36. Reed, E. N.: Infant Disemboweled at Birth, J. A. M. A. **61**:199 (July 19) 1913.
37. Vignard: Lyon mèd. **114**:1054, 1910. Barillet, M.: Thèse de Paris, 1907. Gohl, L.: Inaugural Dissertation, 1912.
38. Farr, quoted by Wheeler, B. B.: W. Virginia M. J. **41**: (June) 1917.
39. Finney, J. M. T.: Old Dominion J. Med. & Surg. **10**:153, 1910.
40. Helmholz, Henry F.: Minnesota Med. **7**:187, 1924.
41. Deaver, H. C.: Appendicitis in Childhood, J. A. M. A. **55**:2198 (Dec. 24) 1910.

No child should be allowed to have a second attack of appendicitis.[42] Suspicious cases should be seen every five to six hours (footnote 4, second reference), and when doubt exists in the mind of the physician, operation is probably the safest course. Drachter [43] rightly says that the problem of appendicitis in the young child is one of diagnosis, and that, if operation is performed before there is general peritonitis or pocketing of pus in numerous places, the mortality of appendicitis should be no greater, but should be even less than it is with the adult.

History of previous attacks is generally unreliable in young children, but occasionally it is strongly suggested. Only 6 per cent of fifteen patients under 5 years of age at the Mayo Clinic [40] gave a history of previous attacks. In thirty-eight of Richter's [44] series of 172 cases (including children over 5 years), or 22.09 per cent, there was a history of previous attacks of appendicitis. The history of the onset may assist in the differentiation from measles, typhoid or rheumatic fever. While most writers believe that the onset of symptoms is gradual, some feel that it may be sudden.[45]

Pain is one of the cardinal symptoms of acute appendicitis in young children. It is regularly present though it may be denied through fear.[46] In 90 per cent of Bolling's series (of children up to 15 years) the initial symptom was pain. Usually the pain is at first general and is referred to the epigastrium or around the umbilicus. It may, however, begin in the right lower quadrant,[44] and increases in intensity in from one to three hours. Richter [44] made a study of the pain in children (including ages above 5 years). Generalized abdominal pain was the first symptom in 137 cases, or 95.1 per cent of his series, and was the second symptom in 4.8 per cent, and the third symptom in 0 per cent. Generalized pain of dull or colicky nature was present in 79.5 per cent and absent in 20.4 per cent. The pain localized itself to the right lower quadrant in 154 cases, or 88 per cent, and failed to do so in 12 per cent. Localized pain in the right lower quadrant was the first symptom in 22.7 per cent, the second symptom in 31.8 per cent, and the third symptom in 45.4 per cent of the cases. The pain settled to McBurney's region on the first day in 70.7 per cent of the cases, on the second day in 17.5 per cent, and on the third day in 10.3 per cent. In short, the pain settled to McBurney's point in 80 per cent of the cases. These percentages would doubtless be lower if the ages were limited to under 5.

Howland,[46] in observing that the appendix is relatively long in children, says that when there is a concomitant, even if localized, peritonitis,

42. Addison, O. L.: Hospital **7**:33, 1911.
43. Drachter, quoted by Howland: München Med. Wchnschr. **65**:1043, 1918.
44. Richter, Harry M.: Abt's System of Pediatrics, **3**:451.
45. Clopton, M. B.: J. Missouri M. A. **12**:94, 1915.
46. Howland, John: Medical Aspects of Acute Appendicitis in Children, J. A. M. A. **83**:962 (Sept. 27) 1924. Collinson, H.: Practitioner **87**:61, 1911.

the pain may be low down in the pelvis or high up in the abdomen or in the back. It may even be on the left side.[41] Howland adds that "in a child too young to localize the pain, it may be inferred from constant crying and restlessness, and from the fact that he sleeps badly." The child with febrile diseases may sleep for long stretches, but the child with abdominal pain will not sleep and will not let anyone else sleep (Howland). The pain may be slight in what Kelly[16] describes as the "larvate form."

The observations of Muller and Ravdin[47] are of interest. They say, "many writers on the subject have erroneously stated that the pain of appendicitis in children varies because of the variations in the position of the appendix, depending as it does, on the rotation of the colon and the descent of the cecum. This is, however, fallacious since the appendix receives its nerve supply through the abdominal sympathetic in embryonic life. This innervation is constant, and does not depend on the anatomic position of the appendix. Disturbed action of the sympathetic nervous system as the result of a lesion in the appendix is the chief cause of symptoms as long as the inflammation is localized to the appendix. The sympathetic fibers make constant connections with the various spinal segments. Since the sympathetic does not contain pain fibers, the sensation of pain is in some way associated with a reference of the stimulus to the cutaneous distribution of the spinal nerves, with which the sympathetic makes its central connection.

Hurst has pointed out that tension is the only adequate stimulus that produces true visceral pain. Therefore, it is probable that tension within the appendix initiates the stimulus that calls forth the sensation of pain in the terminal distribution of the tenth and the eleventh intercostal nerves. Pain, then, which is an invariable symptom of appendicitis, is at first referred to the region of the umbilicus. When the inflammation spreads to the contiguous structures, the pain is felt in the right iliac fossa or in whatever location the appendix happens to be. It is this secondary pain that is diagnostic as to the exact anatomic position of the organ. The pain is an expression of an irritation of the somatic sensory nerves and the result of inflammation of the subperitoneal tissues.

Pain is, of course, encountered frequently in childhood at the onset of such illnesses as the acute exanthemas, respiratory infections, indiscretions of diet, and gastro-enteritis.[40] Some writers even go so far as to say that pain is of little value in the diagnosis of appendicitis in children.[48] Restlessness, irritability, and the character of the child's

47. Muller, G. P., and Ravdin, I. S.: Acute Appendicitis in Children. J. A. M. A. **82**:1852 (June 7) 1924.

48. Chabot, T.: Thèse de Bordeaux, 1914.

cry have been useful in the determination of pain.[49] Pain may be absent.[44]

A very important sign is that changes of position or being moved [49] are resented by the child. Howland [46] believes that the assumption of the sitting posture without complaint argues strongly against appendicitis. Children with a spreading peritonitis will not move unless absolutely necessary. The following case is illustrative of this point.

M. B., a girl, aged 5, four days previous to admission to hospital complained of generalized abdominal pain. Nausea and vomiting followed and persisted. Later, the pain became more localized in the right lower quadrant. The temperature was 101 F., the pulse 120. A leukocyte count was made but was not recorded. The child resisted all efforts to change her position and lay quietly on her back. The patient was first seen by me two hours previous to operation.

Operation.—On opening the abdomen, free purulent fluid escaped. The visceral and parietal peritoneum was markedly injected. Gangrenous retrocecal appendix with perforation at tip was seen. The closure was made with drainage. At the end of the operation, the pulse was 160, and 500 cc. of dextrose Ringer's solution was given by hypodermoclysis. The child regained consciousness and the pulse fell to 120. Despite fluids and stimulants the child's condition gradually became worse and she died twelve hours after operation. Necropsy was not performed.

The pathologist's (Dr. J. C. Williams) examination of the appendix was: "A small appendix, 4 by 1 by 0.8 cm. in the maximum, the serosa reddened and the distal 1 cm. coated with a gray, fibrinopurulent exudate. The lumen contains mucus, bloody fluid, and in the distal 1 cm. of necrotic material and a rough angular fecal concretion 0.7 by 0.5 by 0.4 cm. It was not examined further. Diagnosis: Acute fibrinopurulent appendicitis."

Pain at the umbilicus or during micturition has been said to have more weight than the absence of tenderness in the right flank and muscular defense (footnote 49, second reference). Painful defecation and urination [50] is often an important symptom. In Churchman's [51] celebrated case, a boy was sounded for vesical calculus because of painful voiding.

Holt [49] believes that vomiting is probably the most constant symptom. Finney [39] says that it precedes pain. Some regard it as the most frequent initial symptom.[52] Beekman [53] found that of forty-three cases of appendicitis under 5, thirty-six were ushered in with vomiting. There may be nausea alone. In Richter's study of vomiting as a feature of appendicitis in children (including those over 5 years), vomiting was present at the onset in 79.1 per cent (of 192 cases) and absent in 20.8 per cent. Vomiting was the first symptom in 11.1 per cent of the cases; the second symptom in 71.7 per cent of the cases, and the third in 17.1 per cent of the cases. Emesis was present on the first day in 81.5 per cent of the cases, on the second day in 14.1 per cent, and the third day in 4.2 per cent.

---

49. Holt, J. E.: Diseases of Infancy and Childhood, New York, D. Appleton & Company, 1913, p. 1116. Van Winiwarter, H.: Scalpel **66**:709, 1913-1914.
50. Dowd, C. N.: Arch. Pediat. **27**:226, 1910.
51. Churchman, J. W.: Bull. Johns Hopkins Hosp. **20**:31, 1909.
52. Boulanger, Gaston: Thèse, Paris, 1913. Soltmann and Plettner: Deutsche med. Wchnschr. **35**:1591, 1909.
53. Beekman, F.: Ann. Surg. **80**:913 (Dec.) 1924.

The vomiting in gastro-enteritis is earlier in onset and often precedes the pain (Collinson). In appendicitis, the vomiting does not bring relief (footnote 52, second reference). In seven of Helmholz's fifty-three cases [40] (including ages over 5) vomiting was absent. In four of Bolling's cases there was no vomiting. In four of Beekman's [53] forty-three cases there was no vomiting. Chabot [48] considers vomiting an unreliable symptom.

Constipation is more frequent than diarrhea, but the latter is not uncommon. In Richter's cases, 41.8 per cent were constipated and 17.5 per cent had diarrhea.

What has preceded pertains to information from the history as obtained from the parent or child. Considerable may be learned by inspection. Save for the later stages, the child with appendicitis does not appear to be acutely ill. "He is usually pale; he lies quietly; often dislikes to move the right leg, and keeps the abdomen as quiet as possible by breathing costally." [46] The right or both knees may be drawn up. In cases of suspected appendicitis, Wolf [54] puts the small child on the floor and watches as he runs toward his mother. The psoas symptom becomes evident, while it is frequently lacking when the child is in bed because of the analgesic influence of the doctor's presence. There may be a dragging of the right leg in severe cases.[55]

METHODS OF EXAMINATION

The greatest tact, patience, and strategy [56] must be employed in the approach to and during the physical examination. A proper diagnosis and not infrequently the life of the patient is dependent on the finesse and skill of the examining surgeon. The entire campaign should be conducted so as to put the child at ease. The first step is the interview with the parents before seeing the child. This should be characterized by a kindly seriousness and by sympathy. The surgeon may "hope that it is not appendicitis," for all too often the laity conclude that the calling of a surgical consultant means that operation will certainly eventuate. Once the parents' apprehension is somewhat allayed, the child will be free from the contagion of anxiety in their faces. Be sure to learn the child's first name.

On entering the child's room, avoid a too boisterous "Pollyannaism." A quiet friendliness is the better plan. I believe that it is often useful to become interested in a toy or picture and let the conversation become general about this object rather than about the child himself. In some children such an artifice may arouse suspicion and it is best to come to the point—the "tummy ache" which you were called to make better. If

54. Wolf: München. Med. Wchnschr. **72**:304 (Feb. 20) 1925; abstr. J. A. M. A. **84**:1313 (April 25) 1925.

55. Manning, J. B.: Northwest Med. **6**:307, 1914; Pediatrics **26**:592, 1914.

56. Nageotte-Wilbonchewitch: Bull. Soc. de pediat. **15**:229, 1913.

possible, have a little talk with the child on any subject or about his illness before making the examination.

If he will do so, have him indicate the site of the pain.

For the examination the child should lie flat on his back with the legs out straight and the head may be on a pillow. He may become interested in a toy which he holds in his hands. Be sure that the examining hands are warm. At first, just gently lay the palm of the hand on the abdomen in various places without making pressure. Then, avoiding the right lower quadrant, make gentle pressure in the other quadrants where there is not likely to be tenderness. The child who is naturally apprehensive of pain will thus become less fearful and more cooperative. Cautiously approach the right lower quadrant. Using two hands, one placed over the other, probably gives a better tactile perception. The hand should not be removed from the abdomen during a prolonged examination.[52] The sudden removal of the finger tips may be more painful than the finger tips themselves. Elevation of the knees is not of definite assistance to muscle relaxation unless the knees are supported by the nurse so as to relax the psoas muscles. It is often extremely difficult to get any information at all. As Howland [46] says "the child may refer pain, wherever situated, to the abdomen, usually the whole of the abdomen. He cries whenever touched. If he is old enough to speak, he maintains vociferously that all palpation in painful. He holds the abdomen as rigid as he can, and every attempt at approach is met with resistance. The ordeal is trying on the patient, on the family, and on the physician and is concluded as speedily as possible."

The abdomen is better palpated on inspiration. Holt [49] says that it is practically impossible to make out localized tenderness in any child under 3 years. Farr [57] counsels patience and suggests palpation in a warm bath in the case of a nervous child. It is occasionally possible to examine a child while he is asleep. Examination under ether may be necessary to have proper relaxation. This has been suggested by Gibb,[58] Gardner,[59] Kelly [16] and Finney.[39] The latter is prepared to operate should the examination under ether indicate it, as is also recommended by Helmholz.[40]

When there is definite tenderness in the right lower quadrant in the region of McBurney's point, it is the most conclusive single bit of evidence in making the diagnosis of appendicitis in infants. This view is also held by Helmholz [40] and by Bolling (footnote 4, reference, 3). The tenderness may be on the left.[41, 53] There may be an hyperesthesia of the skin. A retrocecal position adds difficulty to the detection of tender-

57. Farr, C. E.: Arch. Pediat. **36**:207 (April) 1919.
58. Gibb, R. B.: J. Kansas M. Soc. **9**:91, 1909.
59. Gardner, C. B.: J. Mich. M. Soc. **12**:537, 1913.

ness (Bolling). The following case is typically illustrative of the value of localized tenderness in the right lower quadrant.

T. S., a boy, aged 2 years, was admitted to the Evanston Hospital on Oct. 5, 1924. The infant had been ill for three days previously with abdominal pain, nausea and vomiting. On admission, the patient appeared to be acutely ill. The lips and tongue were dry, the face drawn, and the demeanor lethargic. The examination was negative save for the abdomen. There was generalized tenderness and rigidity over the entire abdomen but these were greatest in the region of the appendix. On admission, the white blood count was 21,600. Urinalysis was negative. The first recorded temperature of 103.4 F. was postoperative.

Operation.—This was performed the same day under nitrous oxide and ether anesthesia. On opening the abdomen through a right rectus incision, free pus was encountered but it was generally confined to the lower part of the abdomen. The appendix, which was found to have perforated, was removed. Closure with drainage was made by three cigaret drains.

The patient left the table in poor condition with a pulse of 160, which, however, soon fell to 138. Proctoclysis of 2 per cent sodabicarbonate and 5 per cent of glucose was started. The first days of the convalescence were stormy. The continuous and marked abdominal distention was combatted by external heat, turpentine stupes, pituitary extract and the rectal tube. The stomach was washed out. Fluids were given by hypodermoclysis and proctoclysis. On the fourth day postoperative the patient was distinctly improved, and from then on progress was rapid. The draining wound closed gradually and was finally healed on November 10, thirty-six days postoperative. The child was discharged in excellent condition on November 13.

Pathologic Report (Dr. J. L. Williams).—"An appendix 6.3 by 1.0 cm. in diameter is seen, with a hemorrhagic serosa except at the tip, where it is coated with a patch of fibrinopurulent exudate. The lumen contains a fecal concretion 1.5 cm. long and 0.6 cm. in diameter, together with blood tinged fluid, necrotic material and pus. The lining mucous membrane is hemorrhagic and necrotic. Diagnosis: Acute fibrinopurulent and hemorrhagic appendicitis."

The demonstration of right sided involuntary rigidity or muscle defense is an extremly important diagnostic factor.[47] The right rectus may be held more rigid than the left, or there may be generalized right lower quadrant rigidity. The examination for rigidity should be made with light pressure.[46] Cope [60] asserts that rigidity is a common sign, not of appendicitis, but of the accompanying parietal peritonitis. Muscular rigidity is only found in the active stage of parietal peritoneal inflammation. When the infection becomes localized, the rigidity tends to diminish. There may be absence of rigidity. This has been accounted for in the severe cases by a leakage amid the coils of intestines or against a silent area of the parietes.[60] The muscular rigidity may often be estimated between the child's cries on its deep inspirations.[5] Rigidity was present in 94.9 per cent of Richter's cases.[44]

Rectal examination must never be omitted in doubtful cases. Howland [46] says it should never be omitted in any case. It is of value in determining a retrocecal, a pelvic, or a left sided appendicitis.[61] The confidence of the patient is particularly essential for a successful rectal

60. Cope, V. Z.: Lancet **1**:415 (March 4) 1922.
61. Wachenheim: Arch. Pediat. **33**:197 (March) 1916.

examination.[40] Not infrequently, especially in the cases which are further advanced, a mass may be palpated. Such a mass is composed of the omentum wrapped about the inflamed appendix or it may represent abscess formation. In cases in which there is a considerable abscess formation or agglutination of the omentum and intestines, a definite area of dulness may be present. The following is a case in which dulness played a rôle in the making of the diagnosis.

J. G., a girl, aged 5, twelve days before admission to the Evanston Hospital became ill with diarrhea and acute cramp-like unlocalized abdominal pain. This lasted more or less continuously; three days before admission the child had a sudden acute exacerbation of the pain, with distention of the abdomen and the development of generalized tenderness. The temperature had varied around 101.2 F. On admission, the physical examination was negative save for the abdomen which was distended and rigid throughout. There was a rather large area of dulness in the lower right quadrant, but no masses were palpable. The leukocyte count was 34,000. The temperature was 101 F., pulse 104, respirations 26. Urinalysis was negative.

Operation.—On the day of admission, May 30, 1922, a large, walled off abdominal abscess of the lower right quadrant was opened through a right rectus incision. A large amount of thick green pus was evacuated but the appendix was not identified. Three soft rubber drains were inserted. Hypodermoclysis of 100 cc. was given in the operating room. The convalescence was satisfactory until June 13, when it was necessary, under gas, to insert a finger in the wound to release an accumulation of pus. From then on progress was rapid and the patient was discharged on June 27. Three years later the patient was seen and found to be a robust girl in excellent general condition.

Tympanites, when present, is generally indicative of a more extensive peritoneal involvement. Of some interest is the observation of Ochsanius [62] of the right knee jerk in a child, aged 2 years, which was weakened during the attack of appendicitis, but which was equal to the left reflex after recovery.

Howland [46] says that elevation of temperature is a constant accompaniment of appendicitis, and absent only in the stage of collapse. Others consider it unreliable.[63, 19, 53] In young children, it is generally somewhat higher than in adults and older children but rarely exceeds 102 F. It may be normal. Chills are rare. The pulse in general corresponds with the temperature. Of interest is Von Bokay's [63] observation of bradycardia in children, aged from 7 to 13, with appendicitis.

LEUKOCYTE COUNT

The leukocyte count is of the highest diagnostic importance. The average count in Richter's [44] cases was 21,500; in Muller and Ravdin's [47] series, 16,920. Ninety-five and five hundredths per cent of Richter's cases had leukocytosis, 3.1 per cent a normal count and 1.2 per cent leukopenia. The counts may be very deceptive. Bolling had a leukocyte

62. Ochsanius, K.: München. Med. Wchnschr. **72**:694 (April 24) 1925.

63. Von Bokay, J.: Deutsche med. Wchnschr. **34**:649, 1908.

count of 4,300, with a polyneucleosis of 64 per cent in a 4 year old child, with a grossly ruptured appendix, an abscess and spreading peritonitis. He also had a patient with a 42,000 count with 95 per cent polymorphonuclears in a child, aged 5, with a small well localized abscess. Both children recovered. Speed [25] finds a high count of 10,000 to 35,000 equally in ruptured and unruptured cases. Counts of below 10,000 were found nine times as frequently in unruptured appendixes as in ruptured. The white and differential counts have diagnostic rather than prognostic value.[53] A low count without polyneucleosis generally excludes acute appendicitis. "Eight thousand leukocytes with 85 to 90 per cent of polymorphonuclear cells is very suggestive of appendicitis, especially if the eosinophiles are absent." [40] One should avoid being lulled into security by a low count.

Stengel and White [64] made a study of the leukocyte counts in various diseases in children. For pneumonia, they found a count of 29,000 with a high polyneucleosis. In typhoid, the count was 6,900 though it was raised to 13,000 after a tub bath. In pertussis, 12,000 (much higher counts have been recorded) and in varicella 7,400. Tuberculous caries gave 20,500 with a 75 per cent polyneucleosis, and rheumatism 7,000. Bronchitis was 14,000 with 63 per cent, pleural effusion 13,000 with 32 per cent, and rhachitis 11,900 with 42 per cent. Three counts in cases of enteritis gave 27,000 with 29 per cent, 16,000 with 76 per cent, and 26,800 with 56 per cent.

One may mention only to condemn Denzer's [65] aspiration of peritoneal fluid in cases of suspected peritonitis in childhood and infancy. Manley [66] recalls that deep puncture with an aspirating needle was recommended at one time.

The differential diagnosis of acute appendicitis in young children is often fraught with considerable difficulty. Early cases are commonly mistaken for "food fever," cyclic vomiting, etc.[67] Smith [68] states that among 200 consecutive infants at the New York Foundlings Hospital dying with gastro-intestinal symptoms and malnutrition, fifteen gave evidence at necropsy of inflammatory changes in the appendix. These inflammatory changes, he believes, occur probably as a result of a final infection of the appendixes in the later stages of a general infection of the gastro-intestinal tract.

---

64. Stengel, A., and White, C. V.: Penn. Univ. M. Bull. **14**:310, 1901.

65. Denzer, B.: A New Method of Diagnosis of Peritonitis in Infancy and Childhood, Am. J. Dis. Child. **20**:113 (Aug.) 1920.

66. Manley, T. H.: Diagnosis and Symptomatology in the Appendicitis of Children, J. A. M. A. **36**:1547 (June 1) 1901.

67. Sheffield, H. B.: Internat. J. Surg. **23**:267, 1910.

68. Smith, G. M.: Inflammatory Changes in the Appendix During Early Infancy, Am. J. Dis. Child. **1**:299 (April) 1911.

DIFFERENTIAL DIAGNOSIS

In 1907, Barillet [69] concluded from his study of operative cases in infants that the number of diagnostic errors was considerable.

While a great many pathologic conditions have been enumerated as causing confusion with acute appendicitis in infants, the differential diagnosis most commonly rests between acute appendicitis on one side, and pneumonia, pyelitis, enteritis, intussusception, and pneumococcus or streptococcus peritonitis on the other. "Appendicitis is often believed to be pneumonia in the infant on account of the frequency of pulmonary disease at this age. With older children, primary pneumonia is frequently considered to be appendicitis."[46] Adams and Berger [70] report that twenty-five patients out of 145 with lobar pneumonia were sent to the Boston City Hospital with the diagnosis of appendicitis. Helmholz [40]

TABLE 4.—*Differential Diagnosis of Pneumonia and Appendicitis*

	Pneumonia	Appendicitis
History	Previous cold or cough; chest pain	Exceptionally, grip; usually none
Abdominal pain	Severe, constant, general	Paroxysmal, less intense, local
Vomiting	14 per cent	70 per cent
Diarrhea	Common	Uncommon
Facies	Appearance of illness, dilatation of ala nasi; flushed	Uncomplicated, not seen; pale
Respiratory symptoms	Shallow abdominal breathing, exploratory grunt, slight dulness (?), distant tubular breathing	Shallow breathing, costal type; none
Abdominal tenderness	Superficial, severe, diffuse, higher in abdomen; no worse on deep pressure	Slight or severe; more marked on deep pressure; local
Rectal examination	Negative	Tenderness on right side
Roentgen-ray examination of chest	Positive	Negative
Leukocytes	20,000 to 50,000 (uncomplicated).	10,000 to 20,000
Temperature	103 to 105 F.	98.6 to 102 F.
Attitude	Irritable and restless.	Lies quietly

has drawn up the points emphasized by Adams and Berger in table 4. This table is made to include certain other points.[46]

The child with pneumonia has a flushed face; he looks really ill, and he is irritable and restless.[46] His breathing is abdominal. The child with appendicitis is usually pale and lies quietly and his breathing is costal. The pulse is higher with pneumonia. Deaver [41] believes that the abdominal tenderness may be made to disappear in pneumonia.

The pain and tenderness of pyelitis may simulate that of a retrocecal appendix. Chills and high and variable temperature are characteristic of pyelitis. The finding of pus or motile bacteria in the urine is, of course, the clinching diagnostic factor. "It must be remembered that painful micturition and pyuria may occur in appendicitis nor does a single specimen of urine without pus exclude pyelitis."

69. Barillet, M.: De quelques erreurs de diagnostic dans l'appendicite chez l'enfant, Thèse de Paris, 1907.

70. Adams, F. D., and Berger, B. J.: Differential Diagnosis of Lobar Pneumonia and Appendicitis in Children, J. A. M. A. **79**:1809, 1922.

Ileocolitis lacks the constant localized tenderness in the right lower quadrant. There may be marked prostration but rarely fever. The vomiting of gastro-enteritis usually subsides after the stomach is emptied, and fever and leukocytosis are generally, though not always, missing. Some of the so-called gastro-intestinal disturbances may in reality be recurring, mild attacks of appendicitis.[44]

Intussusception occurs most frequently in the first 2 years of life. It has a sudden onset with periodic attacks of pain, absence of fever, constipation, blood tinged mucus from the bowels and a tumor. Often there may be no local tenderness.

In acute intestinal obstruction the pain is more severe, there is cessation of bowel movements, tympanites, and vomiting which is more persistent than that of appendicitis. Respiratory infections other than pneumonia may simulate appendicitis. The prodromal stages of acute infectious diseases, measles and scarlet fever, and of acute tonsillitis, may at first be puzzling. History of exposure is of value here. In measles, the Koplik's spots are important, and the white blood count shows a leukopenia, although some contend that in the first four or five days the count may be elevated. Typhoid fever generally, though not always, has a leukopenia, typhoid bacilli in the stools and a positive Widal reaction. Osteomyelitis of the ilium or femur may simulate appendicitis, but here pressure on the bone is painful and in the later stages, of course, the roentgen ray is of value. I have seen a case of transitory acute arthritis of the right hip joint, in which the patient was operated on for appendicitis. The surgeon believed that there might be an inflamed appendix so situated on the psoas muscle as to cause the movements at the hip joint to be restricted and painful. Conversely, in 1881, H. V. Gibney called attention to mistaking appendicitis for hip disease. Psoas abscess may cause diagnostic difficulty. According to Brennemann,[71] patients with pericarditis have been operated on for appendicitis and this writer further states that there may often be abdominal pain in throat infections and in mesenteric lymphadenitis which simulates appendicitis. Attacks of colic are paroxysmal and generally relieved by pressure.[40] Numerous other conditions which may be confused with appendicitis are mentioned in the literature, and include cysts of the mesentery, dermoid cysts with twisted pedicle, intussusception of Meckel's diverticulum, inflammation of Meckel's diverticulum, volvulus, salpingitis, coxalgia, streptococcus peritonitis, pneumococcus peritonitis, and gonococcus peritonitis. In the latter three, the abdominal disturbance is more widespread.

Other conditions which may occasion difficulty are, torsion of omentum, spondylitis, retroperitoneal abscess in iliac fossa, inguinal

71. Brennemann, J.: Abdominal Pain of Throat Infections, Am. J. Dis. Child. **22**:493 (Nov.) 1921.

or femoral adenitis, distention of the urinary bladder, acute pancreatitis, meningitis, pyelonephritis, and vesical calculus and poliomyelitis, helminthiasis, and the vomiting of acidosis (Bolling). Gellhorn and Winslow [72] report a case of purpuric colic which simulated appendicitis. The abdominal symptoms were present for weeks before the skin eruption.

Richter,[44] with considerable justice, makes the discouraging statement that the diagnosis of appendicitis in infants is usually announced at necropsy. To help to remedy this condition, it will be best to consider every young child with abdominal pain and vomiting as a potential case of appendicitis. "It is better to operate on an occasional pneumonia thought to be appendicitis, than to let an acute appendicitis go to generalized peritonitis." [40] The younger the child, the more frequent the confusion with other diseases, the more inaccurate the diagnosis, and as a result of this the greater the mortality. It is more common to mistake appendicitis for other diseases than vice versa.[46]

TABLE 5 (Beekman).—*Showing the Greater Frequency of Perforation with Spreading Peritonitis in Infancy Producing the Higher Mortality*

	Unperforated		Abscess		Spreading Peritonitis	
Series of Children	Per Cent of Cases	Deaths	Per Cent of Cases	Deaths, per Cent	Per Cent of Cases	Deaths, per Cent
Up to 13 years.....	33.1	0	36.4	5.7	30.4	18.2
In first half decade.....	6.9	0	39.5	5.9	53.5	43.5

The problem of appendicitis in the young child is one of diagnosis.[43, 46] The operation should be performed before there is general peritonitis or pocketing of pus in numerous places. Acute appendicitis in infancy is characterized by the insidiousness of its onset, and by its tendency to the rapid formation of gangrene and to perforation. The relative inability of the infantile peritoneum to withstand infection is in part, at least, due to the small size of the omentum. General peritonitis is a much more common sequel than in the adult. In the young child, there are very frequently only few adhesions and scarcely any attempt at localization. In a perforation of the appendix the chief defense, according to Pribam,[73] is by speedy absorption of the exudate. Table 5, which is taken from Beekman,[53] is of interest in this connection.

Helmholz [40] analyzed the cases of fifteen children under 5 years of age at the Mayo Clinic. Total number of cases, fifteen; deaths following operation, three; deaths in which there was no operation, four; cases with appendiceal abscess, five; cases with general peritonitis, nine; mortality of the fifteen cases, 47 per cent. Boulanger [52] collected

72. Gellhorn, W., and Winslow, K.: Northwest Med. **2**:81, 1910.

73. Pribam, B. O.: Zentralbl. f. Chir. **51**:1964; abstract J. A. M. A. **83**:1547 (Nov. 8) 1924.

seventy cases, in which the children, under 5 years, were operated on with twenty-seven deaths, a mortality of 38 per cent. Table 6 from Beekman [53] shows the mortality of the different forms at the various years.

In the forty-three cases there were eleven deaths, or a mortality of 25.6 per cent.

An analysis of seventy of the cases under 2 years collected by Abt [14] appears in table 7.

In 1906, Kirmisson [74] collected twenty-five cases of appendicitis under 5 years, and found that only six patients recovered—a mortality of 76 per cent.

While not directly connected with the subject of acute appendicitis, there may be mentioned the views of McGuire, who believes that appendicitis occasionally is the cause of acidosis in children. He advised appendectomy in children, when hygienic and dietetic treatment have been exhausted without relief, and when no other focus of infection can be discovered. He believes that the roentgen ray has some value in making the diagnosis.

Many writers have called attention to the apparent improvement which occurs after a perforation of the appendix has taken place.[25] Abt [14] refers to this as the "period of deceptive calm."

It goes without saying that in suspicious cases no drugs or cathartics should be given to reduce pain. "No child with abdominal symptoms should receive a cathartic until the possibility of appendicitis has been excluded." Moynihan [75] makes a plea for the curbing of the "philocathartic propensities of motherhood." Cathartics undoubtedly precipitate perforation in many cases.[53]

In 1897, Karewski [76] in his classical paper on this subject, recommended early operation, and this view was echoed by Riedel in 1907.[77] Since then, opinion has been virtually unanimous in advising immediate operation.[78, 44] Early operation for appendicitis is more important in infants than in adults.[49] The younger the child, the greater the urgency of the operation.

While on the operating table, the child's body warmth should be maintained. The simplest operation possible should be done,[79] but gentleness should not be sacrificed to speed. The gridiron incision of McBurney is the incision of choice. Richter [44] believes that the danger of a secon-

74. Kirmisson, quoted by Vincent: Rev. de chir. **34**:44 1906.

75. Moynihan, B. G. A., quoted by Bolling: Brit. M. J. **1**:733, 1921.

76. Karewski: Deutsche med. Wchnschr., 1897.

77. Riedel: München. med. Wchnschr. **54**:2365, 1907.

78. Marvel, E.: Arch. Pediat. **29**:366, 1912. Ritterhaus: Beitr. z. klin. chir. **94**:299, 1914.

79. Rees, W. A.: Brit. M. J. **1**:1460, 1911.

TABLE 6.—(*Beekman*)

Age	No. of Cases in Series	Spreading Peritonitis				Abscess				Unperforated			Mortality Percentage for Series
		No. of Cases	Per Cent	Deaths		No. of Cases	Per Cent	Deaths		No. of Cases	Per Cent	Deaths	
				No. of Cases	Per Cent			No. of Cases	Per Cent				
Second year	1	1	100	1	100	0	0	0	0	0	0	0	100
Third year	10	6	60	6	100	3	30	0	0	1	10	0	60
Fourth year	9	6	66	1	16.6	3	33	1	33	0	0	0	22
Fifth year	23	10	43	2	20	11	47	0	0	2	8	0	8.6

TABLE 7.—(*After Abt*)

	Cases Operated On				Nonoperated Cases			
	Total Cases	Recovered	Died	Mortality per Cent	Total Cases	Recovered	Died	Mortality per Cent
Under 1 year	21	15	6	28	14	0	14	100
1 to 2 years	25	16	9	36	10	2 (?) Deiss[8]	8	80
Total	46	31	15	32	24	2	22	91

TABLE 8.—*Mortality of Operated Cases of Appendicitis (Richter, Cook County Hospital and Evanston Hospital)*

	1 Year			2 Years			3 Years			4 Years			5 Years			Total of 5 Years		
	Cases Operated	Died	Mortality %	Cases Operated	Died	Mortality %	Cases Operated	Died	Mortality %	Cases Operated	Died	Mortality %	Cases Operated	Died	Mortality %	Cases Operated	Died	Mortality %
Richter	0	0	0	1	0	0	0	0	0	2	1	50	4	0	0	7	1	14
Cook County Hospital, collected by Richter	1	0	0	0	0	0	3	3	100	0	0	0	5	1	20	9	4	44
Evanston Hospital, collected by Christopher	1	0	0	2	0	0	5	1	20	3	1	33	7	2	14	14	4	22
Total	2	0	0	3	0	0	8	4	50	5	2	40	16	3	18	30	9	30

dary hemorrhage is greater in a drained right rectus incision than in a muscle splitting incision, although the former incision must frequently be employed in female children or when there is some doubt as to the diagnosis. The advice of Finney [39] sums up the best current opinion. The appendix should always be removed, except in cases of large localized abscesses when its removal would entail extensive soiling of the peritoneum. In the latter condition, the abscesses are simply to be drained and if necessary the appendix may be removed at a later operation. The drainage should be adequate. Dental rubber dam or soft rubber tubes are to be employed. The wound should not be closed too tightly around the tubes.[25] Lilienthal [80] reports the case of a gangrenous appendicitis complicating hernia, occurring in a premature child after birth. The truss had caught the appendix and caused it to become inflammed. The surgeon in this case made no attempt whatever to close the wound, and recovery ensued. Deiss [81] believes that many fecal fistulas are caused by leaving the appendix in and simply draining and also by unsatisfactory closure of the appendix stump. Richter [44] maintains that to leave a sloughing appendix behind is to invite disaster. When operating in the presence of a spreading peritonitis, the appendix should be removed with the least possible disturbance to the abdominal viscera. The inflamed peritoneal surfaces should be handled as little as possible. If possible, small laparotomy pads should be used to protect the relatively unaffected peritoneum. If it may be done easily, the appendix stump should be inverted with a linen suture, otherwise it should be strongly ligated with chromic catgut. Multiple drainage incisions are inadvisable.[82] Ether is the anesthetic of choice.

In the postoperative treatment, the body temperature should be maintained and the patient kept as quiet as possible. Kelly [16] places the child on a Bradford frame. The Fowler position is generally best. Fluids and nourishment must be given promptly. Enteroclysis is not well tolerated in the child,[47] and the best solution of this problem is the giving of hypodermoclyses of 3 per cent glucose solution as recommended by Bolling (footnote 4, reference 3). Lavage with weak soda solution is useful in vomiting and gastric dilatation. Distention is treated by stupes, the electric pad and pituitary extract. Enemas are withheld entirely in the bad cases, or are given only with greatest caution and with low pressure. In desperate cases of ileus, the sewing of a catheter into the small bowel for intestinal drainage as advised by Blake [83] is to be tried.

---

80. Lilienthal, H.: Gangrenous Appendicitis Complicating Hernia, J. A. M. A. **51**:754 (Aug. 29) 1908.

81. Deiss, quoted by Abt: Inaugural Dissertation, 1908.

82. Short, A. R.: Brit. J. Surg. **8**:171 (Oct.) 1920.

83. Blake, J. A.: Ann. Surg. **79**:710 (May) 1924.

CONCLUSIONS

1. The most important factors in making the diagnosis of acute appendicitis in children under 5 years are (*a*) elicitation of tenderness in the right lower quadrant, (*b*) leukocytosis, (*c*) rigidity in the right lower quadrant, and (*d*) abdominal pain, named in order of their value.

2. The diagnosis may be extremely difficult.

3. Acute appendicitis occurring in patients under 5 years is characterized by rapid progress to perforation and gangrene, and has a high mortality.

BIBLIOGRAPHY

Gaucher: Bull. Acad. de méd., Paris **70**:387 (March 20) 1917.

Owen, Edmund: Appendicitis, New York, William Wood & Company, 1924.

Wood, W. A.: M. J. Australia **2**:65 (July 28) 1917.

Perrin: J. de méd de Paris **2**:916, 1912.

Werner, N. L.: Journal-Lancet **33**:231, 1913.

Schivers, H.: Scalpel **66**:595, 1913.

Robinson, B. F.: Kentucky M. J. **18**:242 (July) 1920.

Higgins, T. T.: Brit. M. J. **2**:867, 1913.

Bogert, Van der: Arch. Pediat. **33**:772 (Oct.) 1916.

Remsen, C. M.: Ann. Surg. **56**:911, 1912.

Petrén, G.: Beitr. z. klin. Chir. **76**:600, 1911.

Bettman, H. W.: J. A. M. A. **83**:1216 (Oct. 18) 1924.

Vincent, W. G.: M. Rec. **85**:9, 1914.

Porter, M. F. W.: Indian M. Gaz. **56**:130 (April) 1921.

Suter, A.: Cor-Bl. f. schweiz. Aerzte **49**:411 (March 29) 1919; abstr. J. A. M. A. **72**:1578 (May 24) 1919.

Stephan, Eugene: Thèse, Paris, 1907.

Dubs, J.: Schweiz. med. Wchnschr. **50**:341 (April 29) 1920.

Bower, J. O.: New York M. J. **108**:501 (Sept. 21) 1915.

Neudorfer, A.: Zentralbl. f. Chir. **48**:2 (Jan. 8) 1921.

Bores, D. de B.: Am. J. Dis. Child. **15**:421 (June) 1918.

Comby, J.: Arch. de méd. d'enf. **20**:538 (Oct.) 1917.

Bancroft, F. W.: J. A. M. A. **75**:1635 (Dec. 11) 1920.

Lienhardt, B.: Schweiz. med. Wchnschr. **51**:674 (July 21) 1921; abstr. J. A. M. A. **77**:976 (Sept. 17) 1921.

MacManus, F. W.: Journal-Lancet, **40**:600 (Nov. 1) 1920.

Kiblinger, E., and Kiblinger, A.: New Orleans M. & S. J. **73**:136 (Oct.) 1920.

Denzer, B. S., and Anderson, A. F.: Am. J. Dis. Child. **21**:565 (June) 1921.

Binet, L., and Dubois, G. J.: Presse méd. **29**:625.

Vogel, A.: Arch. f. klin. Chir. **115**:1 (Feb.) 1921.

Doyen, M.: Compt. rend. Soc. de biol. **92**:315 (Feb. 13) 1925.

Turner, G. G.: Brit. M. J. **1**:997, 1915.

Robertson, F.: South. M. J. **14**:897 (Nov.) 1921.

Steichele, H.: Beitr. z. klin. Chir. **125**:607, 1922.

Behan, R. J.: Am. J. M. Sc. **162**:705 (Nov.) 1921.

Gray, A. L.: Virginia M. Month. **47**:538 (Feb.) 1921.

Handley, W. S.: Brit. J. Surg. **12**:417 (Jan.) 1925.

Hofman, A. H.: Deutsche med. Wchnschr. **48**:939 (July 14) 1922.

Lunckenbein: München. med. Wchnschr. **69**:12 (Jan. 6) 1922.

Mixter: J. A. M. A. **83**:967 (Sept. 27) 1924.

deNeen, D. D.: Lancet-Clinic **108**:55, 1912.

Backman, W.: Acta med. Scandinav. **56**:478 (April) 1922; abstr. J. A. M. A. **79**:88 (July) 1922.

Morsaline, P.: Sémana med. **16**:1, 1909.
Mitchell: Brit. J. Child. Dis. **9**:355, 1912.
Savariand, M.: J. de méd. de Paris **25**:633, 1913.
Salzer, H.: Wein klin. Wchnschr. **24**:695, 1911.
Sloan, H. E.: Eclect. Med., Cincinnati **69**:372, 1909.
Goedecke, P.: Deutsche Ztschr. f. Chir. **95**:320, 1908.
Gray, H. M. W., and Mitchell, A.: Brit. M. J. **1**:409, 1914.
Bogart, A. H.: Long Island M. J. **3**:416, 1909.
Campbell, W. F.: Med. Times, **43**:86, 1915.
Berkholz, A.: Monatschr. f. Kinderh. **7**:133, 1908.
Fairbank, H. A. T.: Med. Press & Circular, Lond., 1912, n.s., **93**:664.
Alsberg, G.: Arch. f. Kinderh. **50**:252, 1909.
Beekman, F.; Smith, M. K., and Everinghaus, S.: Am. J. M. Sc. **154**:490 (Oct.) 1917.
DuBose: South. M. J. **9**:332 (April) 1916.
Hadley: Colorado Med. **13**:219 (July) 1916.
Motley, J. C.: J. A. M. A. **67**:1364, 1916.
Zimmerman, J. E.: Inaugural Dissertation, Stuttgart, 1909.
Zoege, Helena: Inaugural Dissertation, Zurich, 1911.
Beekman: Ann. Surg. **79**:538 (April) 1924.
Morf, P. F.: J. A. M. A. **68**:902 (May 24) 1917.
Nash, W. G.: Brit. M. J. **2**:595, 1911.

Correspondence

CONTRIBUTION TO THE RICKETS-TETANY PROBLEM

To the Editor:—In the *American Journal of Diseases of Children* **31**:265, appeared what purported to be an abstract but which was, in point of fact, a criticism of a paper of mine entitled "Contribution to the Rickets-Tetany Problem," which appeared in the *Monatschrift für Kinderheilkunde,* **31**:129, 1925. I feel that I should not allow this criticism to pass without comment in justice to myself and to the clinic with which I have the honor to be connected. The abstract, being brief, is reproduced here.

"This is a discussion, chiefly theoretic, based largely on short abstracts from the work of other men, attempting to relate the problem of rickets to the pancreas. The basis of the reasoning is the finding that in tetany as well as in insulin poisoning, there is hypoglycemia.

The article contains few experimental or original observations."

I should like to say that, in the original paper, an attempt was made to examine the literature which has accumulated with regard to certain phases of the rickets-tetany problem from a new point of view, namely, the possible rôle played by the pancreas in the production of the before-mentioned conditions, but this paper was not by any means simply a recapitulation of the work of other men. The conclusions which were drawn were based on studies which were made by me as follows:

1. The effect of atropin on the blood sugar, blood calcium, galvanic irritability and amylase output in rickets and tetany.

2. Amylase output in tetany.

3. The effect of insulin on the blood sugar, blood calcium amylase output and galvanic irritability in normal children.

4. The effect of sugar on electric irritability and blood calcium in tetany.

5. The seasonal changes in the amylase output in children.

6. The amylase output in rickets.

7. Blood sugar level in tetany.

As far as I am aware from a very extensive study of the literature, no one has undertaken any investigation of the problems enumerated in the foregoing, from 1 to 5 inclusive, under similar conditions. There have been data already reported concerning heads 6 and 7, but since they seemed closely connected with the original work which I did, I repeated them and included a report of the results in my paper.

It will be seen from what I have said that the before-mentioned paper is largely the result of original work, and that the investigations of others have been presented only in order to confirm the point of view which I have taken and to render the paper complete.

CHARLES WALTNER, M.D.,
Johns Hopkins Hospital, Baltimore.

News and Comment

ARCHIVES OF DISEASES IN CHILDHOOD

We are in receipt of the first number of the *Archives of Diseases in Childhood,* issued by the British Medical Association. The editors of this journal are Hugh Thursfield, D.M., F.R.C.P., and Reginald Miller, M.D., F.R.C.P., with the help of H. C. Cameron, M.D., F.R.C.P.; H. A. T. Fairbank, D.S.O., M.S., F.R.C.S.; Leonard Findlay, D.S.C., M.D.; A. Dingwall Fordyce, M.D., F.R.C.P. (Edin.); C. Max Page, D.S.O., M.S., F.R.C.S.; G. F. Still, M.D., F.R.C.P.; John Thomson, LL.D., M.D., F.R.C.P. (Edin.), editor of the *British Medical Journal.* We trust that this journal will meet with the success which one could expect from the high character of its editors and from the association which publishes it.

INFANT WELFARE REPORT, MALAY STATES

The annual report for the year 1924 of the infant welfare at Kuala Lumpur, Federated Malay States, shows an attendance for the year of 9,106 infants, 3,193 children and 4,039 women, making 16,238 in all. Of these, there were 11,300 Chinese, 3,369 Tamils and 582 Malays.

GERMAN PSYCHOTHERAPEUTIC MEDICAL CONGRESS

The German General Medical Congress for Psychotherapy will meet April 17-19, 1926, at Baden-Baden. Among other papers will be discussion of psychotherapy in pediatrics by Professor Gött of Bonn and Professor Hasler of Munich.

AMERICAN PEDIATRIC SOCIETY MEETING

The American Pediatric Society will hold its 1926 meeting at Niagara Falls, May 31, June 1 and 2.

BIBLIOGRAPHY ON PEDIATRICS

We are in receipt of a new periodical from Belgium, the first volume of which appeared under "Repertoire bibliographique sur pediatrie" in 1925. This is a bibliography of articles on pediatrics appearing in the literature. The first number of "Pediatrie," a continuation of the former, contains abstracts of articles. These volumes are published by Oeuvre nationale de l'enfance.

ANNUAL CLINIC, IOWA

The physicians in the state are invited to attend the annual clinic of the College of Medicine of the State University of Iowa at Iowa City, April 13-14, the clinic to be conducted by Dr. Campbell Howard, formerly professor

of medicine at the state university and now at McGill University, Montreal, and by Dr. McKim Marriott, professor of pediatrics at Washington University, St. Louis.

APPOINTMENT TO ILLINOIS POST-GRADUATE MEDICAL SCHOOL

Dr. Ralph H. Kuhns, formerly instructor in pediatrics at the University of California, San Francisco, has been appointed professor and director of the department of pediatrics at the Illinois Post-Graduate Medical School and West Side Hospital, Chicago.

Abstracts from Current Literature

Anatomy and Physiology

RENEWAL OF THE BLOOD. A. LICHTENSTEIN and A. J. L. TERWEN, Deutsch. Arch. f. Klin. Med. **149**:102, 1925.

Litchenstein and Terwen found 135 mg. of urobilin per day and 111 mg. per hundred grams of feces as the average, and 200 mg. per day as the maximum, in the feces of fifteen healthy persons. The excretion varies from day to day. Normal urine contains less than 1 mg. per day. Estimating the amount of blood in a normal adult (70 Kg.) at 3,500 Gm., with a hemoglobin content of 14 per cent, and figuring on the production of 21.1 Gm. of urobilinogen from 21.9 Gm. of hematin (contained in the amount of hemoglobin specified), and on the elimination of 150 mg. of urobilin per day, the whole blood is renewed in 140 days or less. (Eppenger concluded, from the secretion of bilirubin, in sixty to forty-three days.) They compare this normal speed of destruction with that of any given subject and call the ratio an index of the "molting" of the blood. Its formula is: $\frac{70}{P.} \times \frac{100}{Hb} \times \frac{Ur}{150}$ (P = weight in kilograms; Hb. = percentage of hemoglobin; Ur. = daily excretion of urobilin in milligrams). Other signs of increased wastage are the supravitally stained substance in more than 0.5 per cent of the erythrocytes, and the increased bilirubinemia.

[ARCH. PATH.]

THE INFLUENCE OF THE SPLEEN ON IRON METABOLISM. ERNST LAUDA, Wien. Arch. f. inn. Med. **11**:293, 1925.

The iron content of the various organs, particularly the liver, of the splenectomized rat was in no way altered from the normal on account of the splenectomy.

Generalized siderosis takes place only if there is actually pernicious anemia present. In the rat experiment, it cannot definitely be shown that the spleen has any influence whatsoever on iron metabolism in the organs and tissues.

SCHLUTZ, Minneapolis.

POSTEMBRYONAL DEVELOPMENT OF THE HUMAN BULBUS OLFACTORIUS. WEISS-FLORENTIN and BRUNNER, Ztschr. f. Hals-, Nasen- u. Ohrenh. **12**:367, 1925.

At birth, bulbus olfactorius is anatomically fully developed, although the layers are not all well differentiated. Regressive changes occur later in the mitral cells and ventricle rests. The regressive changes in the mitral cells are probably dependent on similar changes in the olfactory mucosa. The cause of changes in the ventricle rests is unknown, as is disappearance of the Koerner cell layer of the cerebellum in later life.

LEWY, Chicago.

Pathology, Bacteriology and Biochemistry

HEREDITARY ABNORMALITIES OF VISCERA; KIDNEYS, IN DESCENDANTS OF ROENTGEN-RAYED MICE. H. J. BAGG, Am. J. Anat. **36**:275, 1925.

The visceral abnormalities in the descendants of a group of mice treated with comparatively light doses of unfiltered roentgen rays on five consecutive

days are mainly defects of the kidney, which may vary from a partial to a nearly complete atrophy of one kidney, to the congenital solitary kidney condition, and to complete absence of both kidneys. The right or left kidney may be affected with equal frequency, and there is apparently no sex difference in this respect. Animals with the congenital absence of both kidneys are born alive and are apparently of average weight and development in other respects. They live for about twenty-four hours. Blindness and various defects of the limbs, syndactylism, polydactylism, and especially club feet, are closely associated with abnormalities of the kidneys. One instance of situs inversus viscerum has been noted. Embryologic studies of young from strains with a high incidence of visceral abnormalities have shown that these defects are associated with blood extravasations, especially in the liver and testes, which are similar to those extravasations closely associated with the production of blindness and club feet. Selection has greatly increased the number of animals with visceral abnormalities in the experimental lines. The visceral defects are definitely inherited, are recessive to the normal, and when considered as one of the manifestations of a general tendency to abnormal structure, they approach the mendelian expectation in behavior. [ARCH. PATH.]

VIABILITY OF BACTERIUM TYPHOSUM IN ICE CREAM. M. J. PRUCHA and J. M. BRANNON, J. Bact. **11**:27, 1926.

One gallon of ice cream mix was sterilized, inoculated with *B. typhosum* and incubated until the bacterial count was about 25,000,000 per cubic centimeter. The mixture was then frozen and immediately put into the hardening room. It was kept at a temperature of about —4 F. Samples taken at various intervals showed a constant decrease in the number of organisms. At the end of two years and four months, after freezing, the presence of living typhoid organisms could be demonstrated.

It is evident that low temperatures such as are used for storing ice cream are not to be relied on in destroying typhoid germs in ice cream.

MORPHOLOGICAL AND PHYSIOLOGICAL VARIATIONS IN THE DESCENDANTS OF A SINGLE DIPHTHERIA BACILLUS. MINOT J. CROWELL, J. Bact. **11**:65, 1926.

From a study of pure line strains obtained by the isolation of a single organism, Crowell draws the following conclusions:

1. Morphologic types of the diphtheria bacillus have no hereditary significance and have no relation to virulence.

2. The descendants of toxic diphtheria organisms may be either toxic or nontoxic.

3. The nontoxic strains are direct mutations from the toxic strains.

4. The nontoxic strains are permanently nontoxic.

WESTLUND, Chicago.

THE PRODUCTION OF ALBUMINURIA BY RENAL VASOCONSTRICTION IN ANIMALS AND IN MAN. ISAAC STARR, JR., J. Exper. Med. **43**:31, 1926.

Experiments designed for the study of a possible association of renal vasoconstriction and albuminuria were carried out with the following results:

1. Intact rabbits receiving epinephrine intravenously exhibited albuminuria.

2. Intravenous injection of epinephrine in anesthetized dogs, whose intestines and spleen had been removed, caused albuminuria precisely similar in onset and course to that produced by compression of the renal artery. Operation alone caused no albuminuria in the majority of the dogs when care was taken to avoid exposure, cooling, or trauma to the kidneys. Some showed a slight albuminuria which cleared up in ten to fifteen minutes, and in a few albuminuria persisted throughout the experiment.

3. Transient albuminuria followed inhalation of carbon dioxide, and likewise bleeding in dogs.

4. Cats aroused to fright or anger showed albuminuria. (Emotional excitement is believed to cause increased liberation of epinephrine.)

5. Transient albuminuria followed administration of epinephrine in men, when signs of renal vasoconstriction appeared, but was absent when signs of renal vasoconstriction were lacking.

Pathologic examination failed to reveal change in the kidneys of the dogs sufficient to account for the results.

The author states that the observed facts may be explained by the conception that renal vasoconstriction causes increase in the duration and extent of the normal intermittent interruptions in glomerular circulation. Permeability of the glomerular membranes is so increased by these lengthened interruptions that when blood flow is reestablished, albumin escapes. He believes that this conception may apply to those albuminurias in man which result from excessive muscular exercise or emotion, or which are produced reflexly. It may explain the occurrence of albuminuria in normal people and in healthy animals. Its possible relation to orthostatic albuminuria is discussed.

THYMECTOMY IN THE RABBIT. CHESTER M. VAN ALLEN, J. Exper. Med. **43**:119, 1926.

It was desired to determine whether the thymus could be completely removed from rabbits of certain ages without producing any serious disturbance of health which would interfere with their use in other experiments, or complicate the interpretation of results.

By an operation which is described in detail, the thymus was removed from fifty male rabbits, thirty-six of which were between 1 and 2 years old, eight which were 3 years old or more, and six were between 4 and 6 months. From ten to twenty-two days later, thirty-six of the surviving animals were inoculated with tumor or *Spirochaeta pallidum* and the others were kept as controls. Twenty-nine of the thirty-six inoculated animals survived, and were observed for periods of from two to seven months. The majority of the uninoculated rabbits were observed for approximately three months.

The study of the effects of thymoprivia was limited to observations on the general physical condition and reaction to disease. The results of observation on the effect on reaction to disease is to be reported elsewhere.

Results: There was an operative mortality of 10 per cent, with an additional loss of useful animals, due to secondary complications, amounting to 16 per cent.

Removal of the thymus produced no appreciable effect on the general health or state of nutrition of the animals during the period of observation. The author states that it is not to be assumed that thymoprivia in rabbits is entirely without effect.

McCLURE, Evanston, Ill.

ELECTRO-ENDOSMOSIS THROUGH MAMMALIAN SEROUS MEMBRANES. III. THE RELATION OF CURRENT STRENGTH AND SPECIFIC RESISTANCE TO RATE OF LIQUID TRANSPORT. TRANSPORT RATE WITH SERUM. STUART MUDD, J. General Physiol. **9**:361 (Jan.) 1926.

The rate of electro-endosmotic flow of fluid through animal serous membranes bathed in buffer solutions of varying types and p_H was proportional to the strength of the current used. The mean rate of transport when these membranes were bathed in serum was about 0.25 cm. per minute per milliampere. Since the functional activity of glands is known to be accompanied by electric current flow, the author believes that these data indicate that electro-endosmotic effects are a factor in glandular secretion.

HOAG, New York.

PHYSIOLOGIC ACTION OF LIGHT. II. DEPRESSION OF ARTERIAL BLOOD PRESSURE. III. EFFECTS ON ARTERIAL BLOOD PRESSURE OF DIRECT IRRADIATION OF BLOOD IN VIVO. IV. EFFECTS IN BLOOD OF IRRADIATION IN VIVO. C. J. REED, J. Physiol. **74**:511, 518, 525, 1925.

Reed found that a beam of light of approximately 100 f. c. intensity, when directed into one or both eyes of a dog under ether anesthesia will cause a pronounced depression of arterial blood pressure. A beam of light from a carbon arc employed in the same manner and giving a total intensity of 1,250 faradic current will produce a more profound depression of blood pressure. More intense light does not produce a change of proportionate magnitude but induces the same degree of change somewhat more rapidly. This effect is not wholly due to nervous factors since bilateral vagisection and section of the optic nerve do not abolish or prevent the effect, although the latter operation does modify it considerably. No positive evidence was obtained that photochemical decomposition liberated any depressor substance into the blood stream. Short ultraviolet rays were not present in either of the two sources of light employed.

Reed states that direct irradiation of blood circulating through a quartz tube interposed in an artery will cause a massive depression of general arterial blood pressure. Animals sometimes die from the shock even when anesthesia has been discontinued. This result may be obtained in irradiation with a carbon arc rich in ultraviolet or with a spectrum from which infra red rays have been filtered (longer than 7,000 Angström units) or ultraviolet rays below 3,300 Angström units. The differences between results obtained with these three spectrums are not pronounced.

A beam of light of approximately 4,000 faradic current intensity projected from the positive electrode of a carbon tungsten arc lamp operated on a 110 volt direct current circuit at 4 amperes and condensed through a quartz lens was directed by Reed on a quartz tube interposed in the carotid artery so that the blood flowing through the tube was irradiated directly. Minor changes in hemoglobin percentage and in erythrocyte count occurred in both irradiated and control dogs to about the same degree so that it is probable that the increase was due to concentration of the blood. There was an absolute leukopenia, a lymphopenia but a relative lymphocytosis. The changes were not due to the anesthetic or to shifting of leukocytes. All available evidence indicates that photodynamic effects are, biologically, stimulators of oxidation; and it is suggested that rays constitute one means of accelerating metabolism, which may, however, proceed to a degree of intensity that is destructive.

[ARCH. PATH.]

AN INVESTIGATION INTO THE ETIOLOGY OF DENTAL CARIES. IV. ACCESSORY FACTORS IN DENTAL CARIES (1) REACTION OF THE SALIVA. (2) ACID RESISTANCE OF TEETH. (3) BACTERIOTROPIC ACTION OF SALIVA. JAMES MCINTOSH, W. WARWICK JAMES and P. LAZARUS-BARLOW, Brit. J. Exper. Path. **6**:260 (Oct.) 1925.

The saliva was more acid in persons subject to dental caries than in those who were immune. The experiments devised to show that teeth have varying powers of resisting acid were inconclusive. The saliva may contain agglutinins against *B. Acidophilus odontolyticus* but in small and probably unimportant amounts. They could not demonstrate any appreciable bactericidal action of saliva against the same organism.

HOAG, New York.

THE INFLUENCE OF THE CONSTITUENTS OF THE THYMUS GLAND CELLS ON THE GROWTH OF YOUNG ORGANISMS. Y. MIYAGAWA and K. WADA, Sc. Rep. Govt. Inst. Infect. Dis., Tokio **3**:42, 1924.

Following intraperitoneal injection into young white rats and dogs of the cell constituents of calf's thymus, there is a remarkable increase of weight when small doses (0.05 Gm. per kilogram) are administered; with larger doses (1 to 2 Gm. per kilogram) growth and development are retarded. Control injections of other organs are without effect except in the case of the thyroid in which, with sufficient doses, growth is retarded. While admitting that these results may be explained as due to the action of specific constituents, the writers believe the main effect to be due to the direct action of the cell constituents, after absorption into the circulation, on the homologous gland — thymus or thyroid — with facilitation or retardation of its function.

H. E. EGGERS.

Nutrition

THE RELATION OF THE ENDOCRINE GLANDS TO THE TEETH IN RICKETS. WILLIAM G. WARD, M. J. & Rec. **122**:743 (Dec. 16) 1925.

The author states that rickets is caused entirely by an endocrine unbalance inherited from the mother. In rickets, together with the bone lesions, we find delayed dentition, also that the teeth rapidly decay. The endocrine glands prominently identified in the development and protection of the teeth are the thyroid, parathyroid, pituitary, gonads, suprarenals and thymus. These glands also govern the calcium content in our bodies. The thymus gland has been found atrophied in cases of rickets and marasmus. Ward also states that rickets is not due to a deficiency in diet, but to a deficiency of the endocrine glands which control the retention of calcium salts in the body. The beneficial results reported from treatment by cod liver oil, roentgen ray, violet ray, the Quartz lamp and sunshine are due really to the stimulation of the endocrine glands. The rays also by their stimulation of the glands raise the blood calcium.

WILLIAMSON, New Orleans.

A NEW METHOD FOR CONCENTRATION OF BACILLI IN TUBERCULOUS MILK. S. R. DOUGLAS and L. J. MEANWELL, Brit. Exper. Path. **6**:203, 1925.

A method of concentration is described by which the microscopic examination of milk for tubercle bacilli is made more reliable. Briefly, the method consists in shaking the milk with oil before the addition of the fat solvent (ether). Practically all the bacilli suspended in the fluid are collected in the

zone between the oily and watery layers. Of thirty samples of tuberculous milk, twenty-six were positive microscopically by this method, while by the routine method tubercle bacilli were demonstrated only ten times.

[ARCH. PATH.]

SEROCHEMICAL INVESTIGATIONS ON FASTING ANIMALS. MASASHI NAKAMMA, Jahrb. f. Kinderh. **108**:195 (April) 1925.

The investigations were undertaken in order to determine what pathologic changes take place in the fasting state because these results would throw some light on what changes probably occur in certain nutritional disturbances, particularly intoxication and decomposition, in which a definite relationship to hunger exists. Rabbits, both adult and young, were used in the experiments, and numerous tables and curves are given in the article to show the results of each individual experiment.

The conclusions were summed up as follows:

1. An increase of the antitryptic power in the serum occurs in fasting rabbits, especially pronounced toward the close of the hunger period.

2. At the onset and in the middle of the hunger period, there is a slight increase in nonprotein nitrogen; but toward the end, especially in the premortal state there is a very marked increase.

3. Repeated oral and parenteral administration of egg white or normal rabbit serum showed no influence on the antitryptic power nor the nonprotein nitrogen of the serum.

4. The titer of various antibodies; precipitin, hemolysin, hemagglutinin and typhoid agglutinin, was, in general, lower and their disappearance faster in the fasting animals than in the control animals, also in each case except with precipitin the titer was slightly lower and fell off more rapidly in young than in adult rabbits.

5. Healthy adult rabbits show a slight permeability of the intestinal wall to foreign proteins.

6. The younger the animal the greater the permeability to foreign protein.

7. In adult as well as in baby rabbits, the permeability of the intestinal wall to foreign protein is definitely increased, and the younger the animal the greater the increased permeability.

8. When the fasting period is terminated, the increased permeability subsides and gradually returns to the normal state.

PARMELEE, Chicago.

POISONING DUE TO WOMAN'S MILK. TOSHIWO TANAKA, Mitt. a. d. med. Fak. d. k. Univ. Kyushu Fukuska **9**:1, 1924.

The so-called poisoning due to woman's milk is seen only in breast fed children. It improves early when breast feeding is given up. Return to breast feeding from the same nurse causes an aggravation of the symptoms. The symptoms have occurred in children aged from 2 months to 14 months, particularly in those who are teething. The symptoms are diarrhea, vomiting, suddenly appearing cerebral symptoms, loss of weight, pallor, delirium. Dyspepsia may last from one day to one month, after which follows delirium, irritability and restlessness. The children become apathetic; the eyeballs react slowly, the eyelids are ptosed bilaterally. This clears up if breast feeding is discontinued. When breast feeding is continued the eyeballs turn upward;

strabismus may occur. The child loses ability to walk, creep, sit or hold up its head; ataxia is noticed when the child grasps its toys. The extremities become weak; patellar reflexes disappear and choreiform-athetotic motor symptoms occur. Coma follows, and spastic paralysis of the extremities or facial paralysis is frequent. Death may follow. If breast feeding is stopped, the symptoms disappear rather quickly except the ptosis and muscular weakness which clear up slowly. This disease resembles the polioencephalitis hemorrhagica, described by Wernicke in his textbook on brain diseases, but is observed in Japan in children only who are breast fed.

EHRMANN, Chicago.

Prenatal Conditions

ACCESSORY LOBES OF THE LIVER. T. S. CULLEN, Arch. Surg. **11**:718, 1925.

Cullen reviews the literature on anomalies in size, position and lobulation of the liver, giving summaries of a large number of cases. He reports a case of an accessory lobe springing from the surface of the gallbladder possessing its own pedicle in which were branches of the hepatic artery, hepatic vein, portal vein and hepatic duct. There are only two similar cases on record. The article is well illustrated by Max Brödel, who contributes an explanation of the gross and microscopic picture of the specimen.

CONGENITAL DEFICIENCY OF THE PERICARDIUM. R. L. MOORE, Arch. Surg. **11**:765, 1925.

Sixty-four cases are on record, and forty-two are presented in summary in this article. In only one case was the defect right sided. In a large number adhesions existed between the heart, pleura, diaphragm and thoracic wall. These defects were associated with anomalies elsewhere in the body in six cases. A case of a right-sided defect in a dog is reported.

N. ENZER.

Pathologic Anatomy

INTERAGGLUTINATION OF MATERNAL AND FETAL BLOOD IN RELATION TO ECLAMPSIA. CATHALA and LERASLE, Rev. franç. de gynéc. et d'obstét. **20**:577, 1925.

Cathala and LeRasle found in ninety-two cases of normal pregnancy that the blood of the mother and of the new-born infant were of different groups in twenty-five; thus there was blood incompatibility in 14 per cent. Of the twenty-nine cases with pregnancy complications, the blood groups were different in the mother and fetus in only 20 per cent. Blood incompatibility was manifest in three of twenty-one pregnant women with albuminuria; in one of four with eclampsia and in one of three with uteroplacental hemorrhage. Evidently incompatibility of the maternal and fetal blood is not responsible for eclampsia or other complications in pregnancy, as in the majority of the toxemias of pregnancy investigated there was no iso-agglutination.

[ARCH. PATH.]

ACROCEPHALOSYNDACTYLIA. J. DE BRUIN, Nederlandsch Tijdschr. v. Geneesk. **69**:2380, 1925.

The author describes in detail two children with a very rare complex of congenital deformities of head, eyes and extremities, to which Apert, in 1906, gave the name of acrocephalosyndactylia. The first child was 7 weeks old, the second 4½ years. The article is supplied with a number of fine photographs and roentgenograms.

VAN CREVELD, Amsterdam.

Diseases of the New-Born

PHYSIOLOGIC PIGMENTATION OF THE NEW-BORN. HINES M. ROBERTS, J. M. A. Georgia **15**:4, 1926.

The study of the spinal fluid and blood serum of 423 new-born infants is reported. Bilirubin was found to exist constantly in both, and in the spinal fluid gave a definite xanthochromia varying in intensity from a pale to a deep yellow. The presence of this pigment is not dependent on the existence of macroscopic blood in the spinal fluid, although it is undoubtedly intensified by it. The author reported the incidence of 14.1 per cent intracranial hemorrhage in this series, and stated that it was his opinion that icterus neonatorum is not dependent on the presence of blood in the spinal fluid. He concludes that xanthochromia of the spinal fluid in the new-born is a physiologic condition, and is in no way related to hemorrhage or to other pathology in the central nervous system. Its presence is additional evidence of a general blood destruction beginning in the fetus and continuing for a time after birth.

MASHBURN, Atlanta.

BLOOD GROUPS IN MOTHERS AND CHILDREN. V. OHNESORGE, Zentralbl. f. Gynec. **49**:2884, 1925.

Ohnesorge's data include 302 women and 250 children (including nine pairs of twins). The congruence or incompatibility in the blood groups in mother and child seems to have no connection with the development or sex of the child nor with the toxicoses of pregnancy. He tested the corpuscles from ten fetuses of the fourth to the sixth months. There was no agglutination in seven cases. Two fetuses of the fourth and one of the fifth month belonged to group II.

[ARCH. PATH.]

ADIPONECROSIS SUBCUTANEA NEONATORUM (SO-CALLED SCLERODERMA). W. L. L. CAROL and F. VAN DER ZANDE, Nederlandsch Tijdschr. v. Geneesk. **69**:1317, 1925.

In this article, a description is given of a child, on whom, three weeks after birth, a swelling of the skin in the back developed, which resembled an infiltration of the subcutaneous tissue. The swelling, of a bluish color, soon appeared also at other places of the skin, partly symmetric. They caused no pain on touching and did not show fluctuation. There was no fever.

After frequent convulsions, the child died when 39 days old. The child was asphyxiated when born, and during the first three weeks he had shown no abnormalities, only occasional nose bleed. Elephantiasis, lipomas, sclerema adiposum neonatorum, sclerema neonatorum and scleroderma neonatorum could be excluded, the latter chiefly by a thorough microscopic and microchemical investigation by Carol. After investigation of a piece of the skin, the diagnosis, fat necrosis with fat splitting, with reactive inflammaton and resorption was made. At necropsy, pneumonia lobularis dextra, bronchitis mucopurulenta, was found.

The name of adiponecrosis subcutanea neonatorum was given to the disease. In accordance with former investigators, the principal cause is ascribed to trauma.

VAN CREVELD, Amsterdam.

TRANSMISSION OF ANTITOXIC IMMUNITY INTO THE SYSTEM OF THE NEW-BORN CHILD THROUGH LACTATION. T. IKEDA, Sc. Rep. Govt. Infect. Dis., Tokio **3**:27, 1924.

Examination of the blood of a colt, new-born from an immunized horse, was found to contain only a minimal quantity of diphtheria antitoxin. Following nursing from the immune mother the antitoxic content rose markedly, hence the author deduces that the immunity is transferred by the milk rather than via the placenta. It was found impossible to transfer antitoxin in milk through gastro-intestinal absorption to animals of heterologous species.

H. E. EGGERS.

Acute Infections

TROPICAL SPRUE IN A CHILD SIX YEARS OF AGE. GERTRUDE JOHNSON and F. J. BREIDIGAM, Bull. Battle Creek Sanitarium and Hosp. Clin. **21**:1, 1926.

A case of tropical sprue is reported in a child, aged 6 years, including animal inoculation of *Monilia psilosis* both from the patient and from the necropsied animal, with photomicrographs of the parasites as stained in tissue. The symptoms were those of fever with acute diarrhea, weakness, loss of weight, and no pain, which continued into chronic diarrhea over a period of five months, alternating with constipation. The stools were unusually bulky, whitish in color, pultaceous, yeasty, foamy and had the odor of sour spoiled cheese. The patient had ulcers in the floor of the mouth and the under surface of the tongue which healed and recurred. The tongue was coated. Weight of the child was 27½ pounds. The treatment consisted of cleansing enemas followed by liquid culture of *B. bulgaricus* and *B. acidophilus* to retain; 3 ounces of the same by mouth three times a day. The diet consisted of acidophilus buttermilk and bananas; a glass of buttermilk every hour and six to twelve bananas daily; later green leafy vegetables and baked potato were added. One drop of iodine three times daily and increased to sixteen drops three times daily was begun later. Autogenous vaccine every third day was given but not until the child had shown marked improvement. Eight months after treatment was begun, the child seemed normal in height and weight. The stools also seemed normal.

EHRMANN, Chicago.

THE PRINCIPLES OF IMMUNITY APPLIED TO INOCULATION AGAINST DIPHTHERIA. A. T. GLENNY, J. Hyg. **24**:301, 1925.

The injection of an antigen into a nonimmune animal acts as a primary stimulus. Injection into an immune animal acts as a secondary stimulus to which the response is greater and more rapid. The potential immunity produced by a single injection of toxin continues throughout life although the antitoxin content of the plasma is gradually lost. The natural antitoxin content of the plasma of normal persons is the result of recurrent stimuli by small amounts of toxin, and is variable. Guinea-pigs react consistently to the Schick test because they are used at such an early age that they have had little opportunity to acquire any degree of natural immunity. Any antigenic response depends on the immunity state of the individual as well as on the type of antigen. The true test of a toxoid or toxin-antitoxin preparation is the rate at which it immunizes the Schick reactors in a population with a high positive rate.

ARTHUR LOCKE.

OBSERVATIONS ON 6,500 CASES OF LOBAR PNEUMONIA AT THE COOK COUNTY HOSPITAL, CHICAGO. FRANK B. KELLY, J. Infect. Dis. **38**:24 (Jan.) 1926.

In the seven and one-half years from Jan. 1, 1917, to July 1, 1924, there were 6,531 cases of lobar pneumonia at this hospital, with a case fatality of 36 per cent.

The case fatality in the individual years varied between 34 and 41.4 per cent, with the exception of 1921, when only 26.6 per cent died. The decrease in 1921 occurred in both sexes, in negroes and in whites, and in all age groups. The death rate from this infection was markedly lower in the entire country in that year. There was no significant difference in the case fatality for the entire period in the two sexes.

The case fatality among the negroes was from 5 to 13 per cent below that of the whites in the different years. This was due to a lower case fatality in the negroes in the "40 years and over" group. The case incidence among the negroes in Chicago during this period was apparently twice that of the whites.

The age incidence in the 6,531 cases showed a large number in the "under 5 years" group, the fewest in the second decennium, with a steady increase through the "40 to 49 year" group, followed by a decline so rapid that the number in the "60 year and over" group was very small.

The case fatality was lowest in the "5 to 9 year" group, and from that point increased proportionately with the age.

The greatest number of persons with lobar pneumonia entering the hospital during the year was from January through April. The lowest number was in August. The greatest case fatality was in October, the lowest in June, the variation throughout the composite year being from 32.4 to 41.8 per cent.

There was only 5 per cent difference in the total number of case fatalities of the separate wards for the entire period. Differences in individual years were not accounted for on the basis of age.

FURTHER STUDIES ON A DIPLOCOCCUS FROM MEASLES. PREVENTION OF MEASLES BY IMMUNE GOAT SERUM. RUTH TUNNICLIFF and ARCHIBALD L. HOYNE, J. Infect. Dis. **38**:48 (Jan.) 1926.

The serum from a goat convalescing from a reaction, produced by the inoculation of green-producing measles diplococci, protected rabbits against a subsequent injection of infective material from measles. The rabbits injected with normal goat serum and those untreated showed some or all of the characteristics of measles in rabbits, namely, a rise of temperature, Koplik spots and an eruption.

Serum from convalescent goats protected human beings against measles as effectively as measles serum from convalescent human beings when injected on the first and second days after exposure to measles.

By intracutaneous tests in normal rabbits, the serum of goats injected with diplococci from measles, as well as measles serum from convalescent human beings, were shown to neutralize the action of killed measles diplococci, while serum of normal goats had no such effect.

The serum of one immune goat was found toxic to nearly all persons injected with it, but after eight months preservation it appears to have lost its toxic effect.

While these experiments do not furnish conclusive evidence of the protective value of immune goat serum, they warrant further investigation.

KENNEDY, Rochester, Minn.

PYURIA IN INFANTS AND CHILDREN. W. W. ANDERSON, J. M. A. Georgia **15**:9, 1926.

The author reports eighteen cases, comprising two boys and sixteen girls, with the usual textbook picture of so-called pyelocystitis. The patients were treated by irrigating the bladder with a 1:1000 silver nitrate solution. Anderson is inclined to look on pyelitis as a primary infection of the bladder rather than the pelves and kidneys in a large percentage of children, since such good results have been obtained by irrigating the bladder.

MASHBURN, Atlanta.

A COMPARATIVE STUDY OF THE VALUE OF STAINED SMEARS AND CULTURES IN THE DIAGNOSIS OF GONORRHEAL VULVOVAGINITIS. SARA A. SCUDDER, J. Urol. **14**:429, 1925.

The diagnosis in cases of vulvovaginitis should depend on smears and cultures from the urethra, vulva, vaginal introitus; upper vagina and cervix. Smears are best when made with sterile slender cotton swabs which are evenly rolled, not rubbed, over sterile glass slides.

Staining should be controlled by the use of known gram-positive and gram-negative organisms such as staphylococci and *B. coli*. The alkaline modification of Gram's stain can be so standardized as to give consistent results, if standard commercial dyes and acetone are used, if the gram-positive organisms used as controls are young and actively growing, and if the work is done by trained persons.

Persistent extracellular, gram-negative, biscuit-shaped diplococci, in freshly made and carefully stained films from the genito-urinary tract of children, are presumptive evidence of gonococcal infection, even in the absence of confirmatory clinical and cultural findings. The presence of the gonococcus in the genito-urinary tract of children is not always attended by positive clinical signs; nor is there always a predominance of pus cells in those secretions which contain gonococci. Epithelial cells frequently harbor the organisms.

Negative smears, covering a period of weeks or months with negative clinical signs, are consistent with latency, and are not, necessarily, proof of cure.

The modified Thalmann medium as described by Torrey and Buckell appears to be the best differential medium yet devised for the isolation and maintenance of gonococci, both for uniform character of growth and for longevity of young as well as old strains.

Normal ascitic fluid, added to the medium at a temperature of 50 to 60 C., should be the standard type of enrichment, because it appears to be more constant than other serous fluids, both in reaction and in growth stimulating quality. Semisolid hormone medium, reaction p_H 6.7 to 6.9, to which ascitic fluid has been added for enrichment, gives the most uniform results in maintenance of stock strains for periods of four weeks or more.

The fermentation test is at present the only means whereby the gonococcus can be differentiated from other gram-negative diplococci. The gonococcus isolated from infant cases ferments dextrose only, and, in this respect, does not differ from the adult strains.

The possibility of an overgrowth of the gonococcus in plates, by other types of diplococci (gram-positive in our experience) should be ruled out before a case of vulvovaginitis is classed as nonsyphilitic. In thirty cases of gonorrheal vulvovaginitis, no gram-negative diplococcus was found which could be confused with the gonococcus, either morphologically or culturally. In eighteen

negative cases, used as controls, no organism was found which could be classed as *Micrococcus catarrhalis.*

The smear is still the most reliable criterion of gonorrheal infection, but cultural results will be consistently positive if the material is obtained during the acute stage of the disease.

AUTHOR'S SUMMARY.

TREATMENT OF PERTUSSIS BY INTRAMUSCULAR INJECTIONS OF ETHER. JAMES E. POLLOCK, New Orleans M. & S. J. **78**:450 (Jan.) 1926.

One hundred and seven children with pertussis, ranging from 2 months to 9 years of age, were treated with intramuscular injections of ether. The injections were given every forty-eight hours. The amount varied with the age, weight, severity and the results obtained by the first injection. The average dose ranged from 0.5 to 2 cc. No untoward results were observed.

Marked improvement was observed in 50 per cent following the second injection; in 20 per cent following the third injection, and in 20 per cent following the fourth injection. In the remaining 10 per cent from 5 to 7 injections were required before alleviation of symptoms was noted.

ANDERSON, New York.

THE EFFECT OF VARYING INTENSITIES OF HOOKWORM INFESTATION UPON THE DEVELOPMENT OF SCHOOL CHILDREN. W. G. SMILLIE and D. L. AUGUSTINE, South. M. J. **19**:19, 1926.

Children of school age harboring 100 or more *Necator americanus* show a definite gain in weight, height, and in hemoglobin in three months time when all hookworms have been removed by treatment. Children who are not cured but who are reduced to a light infestation show a similar improvement. An infestation of over 100 worms represents definite hookworm disease. Children, whether treated or untreated, show no variation from the normal in their increase in weight or height and no change in hemoglobin when examined after three months interval.

An infestation of twenty-five *Necator americanus,* or less, produces no measurable injury, even to the growing child and should not be considered as hookworm disease but as a carrier state.

SCHLUTZ, Minneapolis.

ACUTE RHEUMATIC FEVER AND CHOREA IN CHILDREN. HENRY C. BUSSIERE and LAWRENCE J. RHEA, Canad. M. A. J. **16**:35, 1926.

This is an analysis of 100 cases from the wards of Children's Memorial Hospital of Montreal. Chorea was associated with acute rheumatic fever in 27 per cent of cases. The figures given in regard to race and nationality are not of special importance, on account of the relative proportions of the various nationalities in the province.

Seventy-three per cent of cases occurred in children between 6 and 12 years, 20 per cent between 12 and 16 years; the youngest was aged 19 months. Chorea occurred in fourteen males and in forty-five females; acute rheumatic fever occurred in twenty-five males, and in sixteen females. Previous attacks of chorea occurred in 44 per cent; 11 per cent gave a history of two or more attacks. Previous attacks of acute rheumatic fever occurred in 49 per cent; 12 per cent of these gave a history of growing pains preceding first attack. Sixty-four per cent of subjects with rheumatic fever showed cardiac involve-

ment of some type, such as, mitral endocarditis, 70 per cent; mitral and aortic endocarditis combined, 12 per cent. Clinically recognizable myocarditis occurred in all cases of endocarditis and in 10 per cent of cases in which a diagnosis of definite endocarditis could not be made. In chorea, mitral endocarditis occurred in 59 per cent; mitral and aortic endocarditis in 4 per cent. Myocarditis occured in all subjects with endocarditis and in 2 per cent of those without any demonstrable lesion of valves.

Relation of Tonsils: In chorea there was involvement of the tonsils in 79 per cent, in acute rheumatic fever of 82 per cent, of cases. In only 3 per cent of this series was there chorea without associated tonsillitis, acute rheumatic fever or demonstrable cardiac involvement. In acute rheumatic fever, there was only one patient without associated chorea, tonsillitis or demonstrable cardiac lesion.

Season: Seventy per cent of all cases occurred during the winter and spring months.

Family History: Only 17 per cent showed any family history of chorea or rheumatism; in the past history, no relation could be established between focal infection of sinuses, teeth, ears, etc., and rheumatic conditions could be established.

No relation could definitely be noted between previous infectious diseases, such as diphtheria, scarlet fever and measles and rheumatic affections. The symptoms in this series were manifested thus: all large joints involved one after another, 56 per cent; ankle and knee, 17 per cent; ankle alone, 17 per cent; knee alone, 5 per cent; wrist alone, 5 per cent. Subcutaneous rheumatic nodules occurred in 17 per cent; in every instance endocarditis was present. Erythema nodosum occurred in 17 per cent of series and purpura hemorrhagica in 4 per cent.

MOORE, Omaha.

RABBITS AND EXPERIMENTAL MEASLES: WITH SOME OBSERVATIONS ON BLOOD COUNTS AND RABBIT TEMPERATURES. W. J. PURDY, Brit. J. Exper. Path. **6**:210-224 (Oct.) 1925.

Scott and Simon (1924) stated that the sustained rise in temperature and the concomitant amphophilic leukopenia, occurring at a certain time in rabbits inoculated with measles virus, were satisfactory criteria of infection with this virus. Purdy was unable to demonstrate any significant changes in temperature and leukocyte counts in rabbits kept under standardized conditions when these animals were inoculated with blood or nasal secretion from measles patients. Two monkeys were used as controls, and both gave an apparently satisfactory positive reaction.

HOAG, New York.

THE PRINCIPLES OF SERUM ADMINISTRATION IN CEREBROSPINAL FEVER AND THE RESULTS OF THE TREATMENT. KSAWERY LEWKOWEZ, Proc. Roy. Soc. Med. **17**: (July) 1925.

This disease must be regarded as a primary ventriculitis, the lesions found in the meninges constituting only a secondary phenomenon. The chief treatment must be to bring about a sufficiently intense serum reaction in the ventricles and to maintain it uninterruptedly for several days, till complete disappearance of meningococci from the ventricular fluid takes place. The application of this principle does not imply that serum should be administered through a ventricular puncture in each case. On the contrary, antimeningococcal serum injected

intraspinally penetrates into the ventricles in four-fifths of the cases. If intraspinal injections give no result, intraventricular injections should be carried out later and in severe cases from the onset. The author gives results obtained in thirty-seven cases in detail. The point must be borne in mind, that often negative results are obtained after intraventricular injections of serum in infants in their first year. In older persons, serum, so long as it is well adapted to the injecting strain of meningococcus and present in the ventricles in adequate concentration, invariably overcomes the infection. The author states that the mortality of cerebrospinal fever may be reduced to 16 per cent, if subjects in whom intraspinal serum injections have failed, are subsequently treated by the intraventricular serum injections and if in severe cases this better method of therapy is instituted from the beginning of treatment.

WILLIAMSON, New Orleans.

THE ALTERATIONS IN CARDIAC FUNCTION IN INFECTIONS IN GENERAL AND IN DIPHTHERIA IN PARTICULAR. S. LA FRANCA, Arch. di pat. e clin. med. **4**:257, 1925.

The behavior of the heart during acute infections depends on several factors: the temperature, the toxins, anatomic lesions and extracardiac influences. The influence of temperature on heart rate is expressed by van't Hoff's law: the speed of vital functions is doubled or tripled for a 10 degree rise in temperature. The effect of toxins varies. The heart rate may be increased as in tuberculosis or decreased as in the typhoid type of fevers. Anatomic changes may precede the infection, the result of previous injury, old age or alcoholism, or may themselves result from the infectious process. The latter changes consist in degenerative and inflammatory lesions in the endocardium, myocardium or vessels. Extracardiac factors influencing the heart action are lesions of the lungs, kidneys or nervous system.

Disturbances of the heart in diphtheria are of various types: disturbances of contractility leading to cardiac weakness, of tonus permitting dilatation. of irritability causing extrasystoles and other abnormal rhythms, or of conductivity leading to heart block. The disturbances may appear early or during convalescence. The severe types are rare, but milder types of irregularity during convalescence, sinus arrhythmia, extrasystoles, etc., are more common. Postmortem changes consist of the various types of myocardial degeneration.

B. R. LOVETT.

ANKYLOSTOMIASIS IN MESSINA (SICILY). L. FACIOLA, Ann. d'ig. **12**:1039-1049, 1925.

This is a summary of a study of sixty-two cases observed by the author. The disease was most prevalent in the country districts, as shown by the following occupations of the observed patients.

Tillers of soil	37	Children	2
Laborers	9	Herbalist	1
Farmhands	8	Gardener	1
Women	3	Waggoner	1

That the summer season shows the greatest number of cases is shown by the number of admissions to the hospital each month for treatment.

Admitted in January	1	Admitted in July	11
Admitted in February	1	Admitted in August	10
Admitted in March	4	Admitted in September	3
Admitted in April	5	Admitted in October	11
Admitted in May	3	Admitted in November	2
Admitted in June	7	Admitted in December	2

The rise in October is explained by the fact that the farmers harvest in September, and so, unless prostrated by the disease, the patients wait until this period is over before seeking treatment.

The chief modes of infection were:

1. Contaminated drinking water (when of common source, several members of same family were stricken).

2. Touching food with unclean, contaminated hands.

3. Cutaneous inoculation (many of the patients wore no shoes or stockings while at work in the fields).

The reasons given for seeking treatment were pallor; weakness; anorexia; dyspepsia; insomnia and unrefreshing sleep; loss of sexual appetite; slight but constant headaches throughout the summer months; languor; fatigue; edema of ankles.

The majority of cases occurred in subjects between the ages of 10 and 36. Adolescence, youth and mature adults appear to have been the most affected. The infection predominated among the males for obvious reasons.

The generally characteristic findings on objective examination were: Poor nutrition though no actual emaciation; skin of lemon-yellow or greenish-yellow tint; eyes sunken; anemia of visible mucous surfaces; edema of ankles, face or hands; enlarged right side of the heart; systolic murmur over pulmonic area; carotid thrill; atony of soft parts; delayed sexual development if infected before puberty.

Examination of the blood revealed an oligocythemia, anisocytosis; poikilocytosis; macrocytes and microcytes; leukocytosis with predominant polymorphonuclear variety; hydremia. Eosinophilia was not a constant finding excepting in the very severe cases.

The stools were lienteric; some tarry; there were many ova of the hookworm and many were observed in the morula stage. Some cases showed the concomitant presence of ova of the *Trichocephalis dispar* and the *Ascaris lumbricoides.*

The predominating picture at necropsy was that of a chronic duodenal and jejunal catarrh, with numerous minute hemorrhagic areas scattered over the mucosa. Faciola believes that the anemia so characteristic of the disease is due to the hemolytic properties of the toxins elaborated by the parasite and not due to local mechanical trauma by the anchylostoma.

For treatment, he advises the use of thymol until the worm is expelled. Strict municipal control of water supply and personal education in hygiene is urged.

ZAMBARANO, Northville, Mich.

CONTRIBUTION TO THE QUESTION OF DYSENTERY CARRIERS IN THE PHILIPPINE ISLANDS. ANA VAZQUES-COLET, Philippine J. Sc. **28**:173, 1925.

The existence of healthy carriers of *B. dysenteriae* in the Philippine Islands has been demonstrated.

The proof was carried out by isolation of cultures which, according to standard methods of identification, proved to be *B. dysenteriae.*

In 3,328 examinations, fourteen carriers were found, of whom seven harbored the Shiga type, six the Flexner type, and one both Flexner and Shiga types successively.

Agglutination tests were performed with the carriers' serums and with the corresponding culture isolated from the carriers, as well as with stock cultures of the Shiga and Flexner types. Usually the serum of the carrier agglu-

tinated its own strain to a lesser degree than the stock cultures, and at times a considerable inhibition zone was noticed with the carrier's serum and its own strain.

All of the cultures belonging to the Shiga type isolated from the carriers were pathogenic for white mice, and some of them were strongly toxic to rabbits. The cultures belonging to the Flexner type, isolated from carriers, were found to be of low virulence. [ARCH. PATH.]

NASAL PRURITUS AS AN EARLY SIGN OF MENINGITIS. GONZALO R. LAFORA, Arch. españ. de pediat. **9**:398, 1925.

Pronounced nasal pruritus is an early symptom commonly observed in meningitis. The author has observed it in all forms of meningitis, and does not believe that it occurs exclusively in meningeal tuberculosis, as is claimed by some authors. It is apparently caused by irritation of the trifacial nerve or by some of its branches. SCHLUTZ, Minneapolis.

THE THEORY OF MEASLES AS A REACTION SICKNESS. W. KELLER and E. MORO, Klin. Wchnschr. **4**:1719, 1925.

Illnesses which owe their origin to the action of the body's specific reaction products on the pathogenic substance are defined as "specific reaction sicknesses," and are especially typified by measles in contrast to diseases such as scarlet fever, diphtheria, etc., which have no normal incubation period and are due primarily to the action of toxins. An antitoxic substance exists in reconvalescence serum in addition to the bacteriolysins. The course of measles is first building up of bacteriolysins, and finally, building up of antibodies for the endotoxins released in the ensuing bacteriolysis.

ACTIVE IMMUNIZATION AGAINST DIPHTHERIA. R. KOCHMANN, Klin. Wchnschr. **4**:1914, 1925.

There is a negative phase, immediately after the injection of neutral toxin-antitoxin mixtures when the susceptibility of the individual to the diphtheria bacillus is increased. ARTHUR LOCKE.

THE EPIDEMIC NATURE OF ANTERIOR POLIOMYELITIS: SPONTANEOUS TRANSMISSION FROM MONKEYS TO GUINEA-PIGS. HUGO PICARD, Ztschr. f. Hyg. u. Infectionskh. **105**:307, 1925.

Picard confirms Neustädter's observation of a spontaneous transmission of experimental poliomyelitis of monkeys to guinea-pigs kept in cages close to those of the diseased monkeys.

HISTOPATHOLOGY OF EXPERIMENTAL ACUTE POLIOMYELITIS (HEINE-MEDIN) OF MONKEYS AND GUINEA-PIGS. HANS GERHARD CREUTZFELDT, Ztschr. f. Hyg. u. Infectionskh. **105**:402, 1925.

Creutzfeldt gives a description accompanied by photomicrographs of the lesions in the spinal cords of the animals used by Picard in his experiments. He emphasizes the importance of edema in the development of the changes. He also comes to the conclusion that in monkeys the neuronophagia is not performed by leukocytes but by glia cells (Hortega-cell). W. OPHÜLS.

THE CEREBRAL SYMPTOMS OF THE FULMINANT TYPE OF DYSENTERY AND EKIRI IN CHILDREN. TOSHIWO TANAKA, Mitt. a. d. med. Fakult. d. k. Univ. zu. Tokyo **1**, 1924.

In Fukuoka, many fulminant cases of dysentery have occurred, associated with cerebral symptoms, which is usually fatal. This condition usually occurs in children aged from 3 to 6 years, the cause and nature of which symptoms have not yet been discovered. Professor Saito considered the cerebral symptoms due to acidosis. Usually, the intracranial pressure is high, as evidenced by lumbar puncture; the Nonne test is also positive. Furthermore, there is a positive Kernig sign and rigidity of the neck, and because of the symptoms following reduction in intracranial pressure, he concluded that the cause of sudden death in these subjects was due to encephalitis.

The symptoms are as follows: General weakness, mild fever and increased bowel movements, which soon become soft and foul smelling and contain mucus and pus. The children usually complain of abdominal pain preceding the bowel movement. The temperature may rise to 39 to 40 C. (102.2 to 104 F.). Sleeplessness, excessive thirst, vomiting, jactitation, increased pulse, increasing weakness and absence of patellar reflexes are also present. The children become delirious, cry out in their sleep and later sink into coma. The reflexes now become markedly exaggerated and convulsive seizures occur, which are usually followed rapidly by death. Convulsions are at first tonic and then clonic in character; death occurs usually within three days and not infrequently within ten hours. Convulsions are usually generalized, but in practically all subjects localized convulsions can also be found. During the convulsion, the most affected group of muscles can be found, and during convalescence paresis of this part can be noticed, which usually improves within a month.

Localized twitchings are noticeable especially in the upper extremities and usually become worse with each attack, finally becoming generalized. Twitchings of the face, mouth and eyelids are also frequently noticed. The increased reflexes disappear shortly after the convulsions cease in the early part of the disease, but later they remain because of the associated encephalitis. The common sequelae are spastic paralyses, aphasia, mental deficiency, epilepsy. Seldom do pareses or contractures remain. Psychic disturbances which occur are: delirium, restlessness, drowsiness, illusions, hallucinations and coma.

The localized cerebral lesions make it reasonable to assume that this disease is associated with encephalitis. Suzuki found hemorrhages and exudation of the leptomeninges. Clinically, the patients most severely ill have the least change in the spinal fluid, and the author considers this due to encephalitis rather than to meningitis. The children usually die before the associated meningeal symptoms arise.

EHRMANN, Chicago.

Chronic Infections

CLINICAL AND SEROLOGIC VALUE OF THE COLLOIDAL BENZOIN REACTION. EARL D. OSBORNE, Arch. Dermat. & Syph. **12**:706 (Nov.) 1925.

The colloidal benzoin test is stated to be superior to the colloidal gold test in its ease of performance, uniformity of result and amount of information furnished. The reaction is not specific for neurosyphilis in the sense that the cerebrospinal fluid Wassermann reaction is. The author thinks the test should have a wide field of usefulness in differentiating general paresis and incipient general paresis from the other forms of neurosyphilis.

CLINICAL STUDY OF KAHN PRECIPITATION TEST AND KOLMER COMPLEMENT-FIXATION TEST. ROBERT LEE KELLY, Arch. Dermat. & Syph. **12**:720 (Nov.) 1925.

Since most of the previous comparisons of the Kahn test with the Wassermann test have been made with a nonstandardized Wassermann test, this study is justified by the use of a standardized test for comparison. In a study of 110 cases, agreement between the two tests was observed in 105 cases (95.5 per cent). Three subjects known to have had syphilis in the past gave a positive Kahn and a negative complement fixation test. One subject known to have had syphilis gave a repeatedly negative Kahn reaction and positive complement fixation test. One subject, probably syphilitic, gave a positive Kahn and a negative complement fixation test.

JEANS, Iowa City.

THE TREATMENT OF SYPHILIS IN CHILDREN. JOSEPH YAMPOLSKY and GEORGE F. KLUGH, J. M. A. Georgia **15**:1, 1926.

Yampolsky and Klugh describe completely their treatment of syphilis in children. They state that they find difficulty in getting into the veins in very young infants, and that intramuscular treatment is not always satisfactory, due to the pain caused to the little infants.

For that reason, one of them, Yampolsky, two years ago, began experimenting by injecting rabbits intraperitoneally with neo-arsphenamine and mercurosal. The doses given were larger than the size usually given to a human being. The idea governing the experiment was to prove that neither of the drugs would cause peritonitis or adhesions, and the rapidity with which these drugs would be absorbed into the blood from the peritoneal cavity. The medications given alternately were neo-arsphenamine and mercurosal. The rabbits that received the mercurosal injections finally died from overdose. Eventually, the proper dosages were selected, being 1/10 of a gram of neo-arsphenamine in 2 cc. of distilled water, and one-half a grain of mercury to every 30 pounds of body weight. Two children were injected and treated intraperitoneally with these two drugs. Fluoroscopic and roentgen-ray examinations after the end of the treatment showed that these patients did not suffer from adhesions or peritonitis; and the structures of the intestinal tract were in normal position. Both patients are alive and well. One has a negative and the other a positive Wassermann reaction.

MASHBURN, Atlanta.

MANAGEMENT OF SYPHILIS COMPLICATING PREGNANCY. A. C. BECK, New York State J. Med. **26**:102 (Feb. 1) 1926.

This is a review of 131 pregnancies in 113 syphilitic women. Twenty-six patients had no previous miscarriages and had given birth to viable and apparently healthy children, but investigation showed that most of their children were syphilitic. Energetic treatment with arsphenamine and mercury was started as soon as the diagnosis was made, irrespective of the period of gestation. Of seventy patients receiving six or more injections of arsphenamine, fifty-eight gave birth to living infants who have never shown any evidence of syphilis, but a guarded prognosis is recommended, as two children recorded as non-syphilitic in a previous report gave the first sign of syphilis at the ages of 3½ and 4 years, respectively.

WILLIAMS, New York.

THE SEMEIOLOGIC VALUE OF THE MAMILLARY EMINENCE AND THE TUBERCLE OF CARABELLI AS SIGNS OF CONGENITAL SYPHILIS. EMILIO JANE, Ann. de dermat. et syph. **6**:734 (Dec.) 1925.

This dental deformity is of diagnostic value, having been found to be accompanied by a positive Wassermann reaction in 60 per cent of a series of twenty-nine cases. Nine of these cases, with negative or doubtful serologic findings, presented other stigmas of congenital syphilis.

HYPERTRICHOSIS OF THE UPPER LIP IN WOMEN CONSIDERED AS A STIGMA OF CONGENITAL SYPHILIS. N. DRACOULIDES, Ann. de dermat. et syph. **6**:745 (Dec.) 1925.

Attributing this condition to endocrinous changes, especially ovarian insufficiency, possibly of syphilitic origin, the author reports having found other signs of congenital syphilis in 22 per cent of a series of fifty patients with this trouble. In a series of known congenitally syphilitic cases, the condition was found in 35 per cent.

UNILATERAL SYPHILITIC HEREDITY. P. GASTINEL, Bull. Soc. franç. de dermat. et syph. **32**:R.N.55, 1925.

In two cousins, whose grandfather was syphilitic, there was hydrocephalus, Little's disease and a positive Wassermann reaction.

ABSENCE OF THE XYPHOID PROCESS AS A SIGN OF CONGENITAL SYPHILIS. LOUIS QUEYRAT, Bull. Soc. franç. de dermat. et syph. **32**:323, 1925.

In the opinion of Queyrat, the absence of the xyphoid process in a given case should lead us to look for congenital syphilitic infection. He cites illustrative cases.

PARKHURST, Toledo, Ohio.

A CONTRIBUTION TO THE KNOWLEDGE OF THYROIDEAL ALTERATIONS IN HEREDITARY SYPHILIS. E. MORELLI, Boll. d. Inst. Sier. Milan **4**:215 (Aug.-Sept.) 1925.

For this histopathologic study, the author has examined the thyroid gland in three groups of cases. In the first group are the thyroids of children dying soon after birth, who had shown evident clinical and anatomopathologic stigmas of precocious heredosyphilis. In these cases the spirochete was found in the liver. In the second group are the thyroids of children who grew normally for a certain period of time, but who at a later age showed signs suspicious of syphilis, the presence of which was confirmed afterward by necropsy. In the third group are the thyroids of children in whom the Wassermann test was positive, but who showed no clinical signs during life and no anatomopathologic evidences of syphilitic infection at necropsy. The importance of this research lies in the fact that the author found not only the usual connective tissue proliferations, but also other important histopathologic changes. In the thyroids from patients with early hereditary syphilis, hyperplasia and anomalies in connective tissue distribution, altered structure of the organ, extensive epithelial degeneration and formation of abnormal colloid was found. In late hereditary syphilis, the thyroid was found to be less involved, but it was in a state of unstable equilibrium, liable to respond in an exaggerated manner to hypersecretory stimuli. There were structural changes but no connective tissue hyperplasia, and there might be epithelial desquamation and

transudation of plasma instead of colloid secretion under excessive stimuli. Associated with a structure that indicates degeneration there is always, at distant points, suggestive evidence of vicarious hyperplasia.

NACCARATI, New York.

THE FLUID FROM INDUCED BLISTERS IN SYPHILITIC INFANTS. M. SOLDIN and F. LESSER, Deutsch. med. Wchnschr. **51**:1817, 1925.

Cantharidin blisters were produced in infants, and wherever there were cutaneous manifestations of syphilis the fluid was found to contain spirochetes. Obviously, cases may occur in which such demonstration might be of conclusive diagnostic value.

[ARCH. PATH.]

BRONCHIAL ASTHMA TREATED WITH INJECTIONS OF TUBERCULIN. C. RAHBEK ØSTERGAARD, Ugesk. f. Laeger **46**:1001, 1925.

Eleven patients with bronchial asthma are reported, who were treated with old tuberculin. Seven of the eleven were free from asthmatic attacks from two to fifteen months, but four showed no improvement.

The treatment was carried out over a period of two months, and the dosage of old tuberculin was gradually increased from 0.0001 Gm. to 0.01 Gm.

The reason for using old tuberculin instead of other foreign proteins containing albumin or casein is to prevent the sensitizing of the asthma patient to protein foods. Moreover, old tuberculin seems more effective than protein solutions in bronchial asthma.

TREATMENT OF TUBERCULOSIS WITH SANOCRYSIN. V. BIE, Ugesk. f. Laeger **47**:1023, 1925.

This is a report of a few cases of acute febrile tuberculosis treated with sanocrysin by intramuscular and intravenous injection, but without the injection of antituberculous toxin serum.

In all cases reported the results were excellent, according to the author. He comes to the conclusion that the serum should not be used, as it increases the tendency to exanthemas and dermatitis.

THE FOLLOWUP OF PATIENTS HAVING LUNG TUBERCULOSIS TREATED WITH SANOCRYSIN. PAUL KÜHNEL, Ugesk. f. Laeger **47**:1036, 1925.

A table is shown in which the patients are grouped according to degree of lung involvement. One month after the twenty patients in group 1 (the mildest cases) were discharged from treatment, the following changes in their condition were noted: nine, markedly better; six better; two, unchanged; and three had died. In the fifteen patients of group 2 (the more severe cases), the following changes were noted: one, markedly improved; two, better; four, unchanged; six, worse; two had died. Group 3 shows that only two out of fifteen patients were improved.

It is evident that the time elapsing between the final treatment and the present report was not long enough to demonstrate any lasting beneficial effects from the use of Sanocrysin. Further, by a critical study of the data, one is not convinced that this heroic treatment is more efficient than hygiene, good food and heliotherapy.

SCHLUTZ, Minneapolis.

Internal Diseases

THE HEREDITARY FACTOR IN PERNICIOUS ANEMIA. E. MEULENGRACHT, Am. J. M. Sc. **635**:177 (Feb.) 1925.

The author premises the fact that the causes leading to many diseases are so intimately connected with hereditary factors that their pathogenesis can be understood only in the light of these factors. He reviews some points of importance in this connection, choosing as a particular illustration pernicious anemia.

For purposes of clarity, he adopts the terminology used in heredity. N. Johannsen has coined the term: the genotype, the external conditions, and the phenotype. The genotype of an individual signifies the basic peculiarities present in the fertilized egg, which determine the individual's possibilities in development. The external conditions are the external influences encountered in life. The phenotype signifies the personal characteristics of the individual resulting from the interaction of genotype and external conditions.

The causes leading to the development of a disease lie partly in external factors. For every characteristic (or disease) the genotype is met in its interaction with the external conditions determining the characteristic (or disease).

The question concerning the evidence of heredity in the incidence of pernicious anemia is considered. The author states that there already exists sufficient material to indicate that the disease may occur with an hereditary incidence, and that this must mean that special elements in the genotype play an important rôle in its etiology. The next problem is whether anything can be learned concerning the peculiarities of the genotype which determine the etiology of pernicious anemia. Two methods are available for this purpose: (*a*) The analysis of causistics. Using this method, one endeavors to follow the hereditary manifestations of disease through a series of generations, and special families are chosen, either because the disease for some reason has been richly represented in the family, or because special conditions have favored an investigation. The method has been severely criticized from a statistical point of view. (*b*) The method of statistical summation. In this method, a single generation is investigated concerning the numerical relation of diseased and sound progeny resulting from those crossing which could give rise to the disease. Because of the paucity of human progeny, however, it is necessary to deal with the average values obtained by a summation of the healthy and diseased progeny in a series of families. This method must also be used with great caution.

From the resulting figures of each method the attempt is made to draw conclusions as to the nature of the genes (inheritance factors) in question.

Applying these methods to the problem at hand, the analysis of casuistics, as applied to pernicious anemia, led Mustelin to offer the hypothesis that the disease is a dominant property depending on a single gene. The method of statistical summation cannot be used because the supply of necessary statistical data does not exist. However, Levine and Ladd conclude that pernicious anemia is hereditary in 6.7 per cent of the cases.

Intestinal parasities, intestinal constrictions and sprue have all been assigned etiologic rôles, but in the majority of cases, no external conditions can be found.

The following theory of its pathogenic nature has been promulgated:

Pernicious anemia is due to a general intoxication which in its later stages affects the blood and blood-forming organs as well as the peripheral nerves, central nervous system, etc. The specific external causative factors in this case merely set to work the same unknown factors that are active in the other forms.

AUGUST, Detroit.

SPLENOMEGALY (TYPE GAUCHER) AND LIPOID-HISTIOCYTOSIS (TYPE-NIEMANN). WILLIAM BLOOM, Am. J. Path. **1**:595, 1925.

Two cases are reported, that of a boy aged 6 years and that of a woman aged 42 years, in whom there was a history of long-standing increase in the size of the spleen, leukopenia, mild secondary anemia, and epistaxis in one case and uterine bleeding in the other.

Microscopically there were large pale cells which contained iron and gave no typical reactions with the usual lipoid stains in the spleen, liver and lymph nodes. These large cells had a marked longitudinal striation with Mallory's aniline blue connective tissue method. These two cases seem to be typical of Gaucher's disease.

Three cases of the condition first described by Niemann are reported in infants aged 18, 14 and 7 months. The history in the first two was of long continued disturbance in feeding and a failure of the infants to develop. The third patient died of meningitis at a comparatively early period in the disease. One case was recognized in vivo, and the patient improved a good deal for two months after splenectomy, but then began to fail again.

Anatomically these cases have a widespread infiltration of lipoid material in the reticulum cells of the spleen, lymph nodes and thymus, Kupffer cells, clasmatocytes of connective tissue, and the large cells in the alveoli and perivascular tissues of the lung. The large foam cells are also present in the arteries of the lungs, pancreas and kidneys, and in the branches of the portal vein. In sharp contrast to the Gaucher cells, these cells stain positively for the complex lipoids; they do not contain iron, and are markedly vacuolated after treatment with absolute alcohol. The absence of the large cells from blood smears can probably be explained on the basis of their being filtered out by the capillaries, especially those of the lungs.

Chemical analysis of these spleens is now under way, and will be reported on elsewhere.

AUTHOR'S SUMMARY.

ABNORMAL ARTERIOVENOUS COMMUNICATIONS, ACQUIRED AND CONGENITAL. THE EFFECTS OF ABNORMAL ARTERIOVENOUS COMMUNICATIONS ON THE HEART, BLOOD VESSELS AND OTHER STRUCTURES. M. R. REID, Arch. Surg. **11**:25, 1925.

Collateral circulation is greater from an arteriovenous fistula than from simple occlusion of a vessel. Proximal to the fistula the artery usually dilates, the walls become thin, and atrophy of muscular and elastic tissue takes place. True aneurysms occur proximal to the fistula. The proximal dilatation may extend back to the heart causing hypertrophy and dilatation. Such vascular lesions often cause increased length of limb especially before the epiphyses are ossified. Beyond the fistula the circulation is impaired. Kidneys of dogs did not survive complete reversal of circulation.

PULMONARY ATELECTASIS WITH SPECIAL REFERENCE TO MASSIVE COLLAPSE OF THE LUNG. E. D. CHURCHILL, Arch. Surg. **11**:489, 1925.

Massive collapse of the lung is a variety of pulmonary atelectasis and probably due to the same etiologic factors, viz.: bronchial obstruction and weakened respiratory force. Nine cases are presented, and common to all of them were weakened respiratory force and bronchial obstruction. Early purulent sputum was present in all post-operative cases and several of them had a history of previous respiratory infection. The weakened respiratory

force may be due to a low physical state or to paralysis or impairment of the respiratory muscles. The right lower lobe was most often affected, and this is attributed to the construction of the bronchial tree which favors gravitation of exudate or secretion to this lobe. Atelectasis most likely does not predispose to pneumonia, nor do emboli appear to be a factor in the etiology. The literature is reviewed.

HIRSCHSPRUNG'S DISEASE, OR CONGENITAL MEGACOLON. O. HOFMANN and G. H. EWELL, Arch. Surg. **11**:674, 1925.

A case of enlargement of the colon in a boy 8 years of age was noted at operation. From the clinical history and appearance at operation the authors conclude that the case was one of congenital megacolon. Death occurred on the thirteenth day after operation, but necropsy was not obtained. They review the literature on the etiology, pathology and clinical treatment.

N. ENZER.

POST-ANAESTHETIC HYPOGLYCEMIA. A STUDY OF THE ETIOLOGY OF RECURRENT VOMITING. HUGH JOSEPHS, Bull. Johns Hopkins Hosp. **37**:376, 1925.

The curve of blood sugar, the excretion of acetone bodies and the respiratory quotients have been studied in a series of children who had undergone short periods of anesthesia. Hypoglycemia of moderate degree was found to occur with great regularity from eighteen to twenty-four hours after the anesthesia. This hypoglycemia was preceded usually, but not invariably, by an increase in the respiratory quotient, and was accompanied by an increased excretion of acetone bodies in the urine. These changes were greater than could be accounted for by starvation. The bearing of these results on the etiology of recurrent vomiting and the allied condition of "post-anaesthetic acidosis" is discussed.

AUTHOR'S SUMMARY.

HYPERTROPHIC PYLORIC STENOSIS IN INFANTS. J. C. WILLIS, SR., New Orlenas M. & S. J. **78**:125, 1925.

The author believes that the condition is due to a primary spasm, and that the hypertrophy of the muscle fiber is secondary. In support of this conclusion, he cites a case in which the clinical picture and roentgen-ray examination were that of pyloric stenosis and which at operation showed a healthy pyloric muscle.

The writer prefers the Rammstedt operation to the more complicated procedure advocated by Strauss.

THE INFANT'S PYLORUS: SPASM AND STENOSIS. FRANKLIN G. RILEY, New Orleans M. & S. J. **78**:345 (Dec.) 1925.

The author discusses the various opinions concerning the etiology of the condition. He emphasizes the importance of preoperative and postoperative treatment and advises the parenteral administration of fluids to combat the dehydration and shock following the operation. He favors the Rammstedt operation in preference to the more extensive surgical procedures.

ACIDOSIS IN INFANCY. ROY E. DE LA HOUSSAGE, New Orleans M. & S. J. **78**:456 (Jan.) 1926.

In severe cases of acidosis, the author emphasizes the value of intravenous injections of 10 per cent glucose solution.

CARDIOSPASM. PORTER P. VINSON, New Orleans M. & S. J. **78**:484, 1926.

The author believes that this condition is due to a disturbance in the nerve-muscle mechanism of the entire esophagus. The term, cardiospasm, should be reserved for those cases of definite obstruction at the cardia demonstrated by the roentgen ray, without anatomic stenosis and with or without dilatation above the point of obstruction. There is no evidence that psychoneurosis is an etiologic factor. The ages of the patients included in the report varied from 5 to 83 years; in one of them symptoms began at the age of 3 years. The three cardinal symptoms were dysphagia, pain and regurgitation. The most efficient treatment has been the forcible dilatation of the cardia.

ANDERSON, New York.

OBSTRUCTION OF THE RENAL TUBULES DURING THE EXCRETION OF HEMOGLOBIN. S. L. BAKER and E. C. DODDS, Brit. J. Exper. Path. **6**:247 (Oct.) 1925.

The authors report two cases in which transfusion of blood was followed by collapse, fever, hemoglobinuria and suppression of urine, both cases terminating fatally. Microscopic examination of the kidneys showed extensive intrarenal obstruction caused by the collection of hemoglobin débris (probably hematin) in the uriniferous and collecting tubules. They point out the similarity to the intrarenal obstruction occurring in blackwater fever. By in vitro experiments they showed that hemoglobin is thrown out of solution when the reaction of the medium is about p_H 6.0 and the sodium chloride concentration is 1 per cent or over. It seems probable that the large amount of hemoglobin liberated by the rapid agglutination and hemolysis of incompatible red blood cells is successfully eliminated from the body in the renal glomerular transudate, but is there precipitated as the p_H and sodium chloride concentrations reach or exceed the figures mentioned. The resulting intrarenal obstruction leads to serious and sometimes to fatal symptoms. On the basis of these findings, the rational treatment is the production of alkaline diuresis.

HOAG, New York.

CYSTIC LYMPHANGIOMA OF THE CHEEK, WITH MALIGNANT DEGENERATION. A. G. WEISS, Bull. Soc. franç. de dermat. et syph. **32**:R.S.158, 1925.

In a child, a lymphangioma of the cheek, in the region of the first branchial cleft, had undergone degeneration which was considered sarcomatous. Prior to the malignant development, roentgen-ray therapy had been used, and there had been an infection of the tumor, necessitating an incision.

[ARCH. PATH.]

CLINICAL FORMS OF DILATATION OF THE BRONCHI IN CHILDREN, AND THE ROENTGEN-RAY DIAGNOSIS FOLLOWING THE INJECTION OF IODIZED OIL. P. F. ARMAND-DELILLE, R. J. LEVY and J. J. MARIE, Rev. franç. de pediat. **1**:125, 1925.

Dilatation of the bronchi in children is a difficult diagnosis, as the classical symptoms of bronchiectasis are rarely seen. The diagnosis is often arrived at through a process of elimination. The intratracheal injection of iodized oil is a method by which the diagnosis can be established.

A systematic study of fourteen cases was made following the technic of Sergent and Cottentot (*Bulletins et mémoires de la Société médicale des*

hôpitaux de Paris, May 11, 1923), except that the oil was injected between the cricoid and thyroid cartilages. Clinically, the cases consisted of those showing a clear cut symptomatology, those of recurrent bronchitis, those showing only an occasional symptom (the formes frustes), and latent cases in which the roentgenogram showed only an abnormal shadow, incapable of definite clinical interpretation. In the latter group, a roentgenogram after injection of the oil showed multiple dilated bronchi at the site of the shadow. In the others, one was able to distinguish cases of true dilatation from those in which the symptoms were caused by enlarged tracheobronchial glands. Various types of dilatation were seen, cylindric, ampullary, etc. There seemed to be no constant relationship between the clinical and roentgenographic findings.

The article is accompanied by seventeen excellent plates.

LESLIE, Chicago.

SOME DEVIATIONS OF HEART AND BLOOD VESSELS IN SCHOOL CHILDREN. J. DE BRUIN, Nederlandsch Tijdschr. v. Geneesk. **1**:2192, 1925.

This is a reprint of a lecture given for school physicians in Amsterdam, in which the author discussed the so-called accidental heart murmurs and palpable thickened arteries in school children. The accidental heart murmurs are very rare in children under 3 years. In school children they are to be divided into four groups: 1. Extracardial, cardiopulmonary murmurs, originating in the lingula of the lung. They occur, according to Schlieps, in about 36 per cent of all the school children and more frequently in girls than in boys. 2. Atonic murmurs of Schlieps in about 18 per cent and in overgrown children. They are intracardial and not accompanied by dilatation of the heart. 3. Pulmonary murmurs of Von Rumpel and Reiche. In children with these murmurs, the retrosternal area differs very much in inspiration and in expiration. During expiration, the pulmonary artery is pushed against the front wall of the chest. The frequency of this condition in children is unknown at present. 4. The anemic or velocity murmurs of Sahli are caused partly by a decreased viscosity of the blood in anemia. They are rare.

The venous murmurs are to be separated from these four groups. They occur sometimes in tuberculous as well as in nontuberculous children.

Palpable thickened arteries were found by the author very often between 7 and 14 years, sometimes accompanied by orthostatic albuminuria, but never by increased blood pressure, hypertrophy of the left part of the heart, chronic nephritis or syphilis. It was improbable that real arteriosclerosis was the cause. The author cites the opinion of Hamburger (1911) that we have to do in these children with an angio-asthenia or cyclasthenia, and abnormal irritability of the circulatory apparatus, which causes an increased arterial tonus in these neuropathic children.

VAN CREVELD, Amsterdam.

PAROXYSMAL HEMOGLOBINURIA. J. ENNEKING, Nederlandsch Tijdschr. v. Geneesk. **2**:1526, 1925.

The special feature was a hemoclastic crisis preceding the attacks of hemoglobinuria in a man, aged 37. The autolysin had hemolytic action in the test tube even without chilling. The attacks of hemoglobinuria seemed to occur exclusively in the night. The man died from necrosis of the bowel.

[ARCH. PATH.]

Nervous Diseases

EXPERIMENTAL TETANY AND DIET. T. INOUYE, Am. J. Physiol. **70**:524 (Nov.) 1924.

In a large series of thyroparathyroidectomized dogs, observations were made relative to the effect on the consequent tetany of certain carbohydrate food stuffs in varying combinations. The carbohydrates used were sucrose, glucose, dextrin, lactose and galactose, given in association with varying amounts of casein. Inouye found uniformly that with diets containing lactose or galactose in minimum percentages of fifteen and twenty, respectively, the development of tetanic manifestations could be definitely prevented. The amount of lactose required was found also to vary directly in relation to the diet protein (casein) content. Of interest also is the fact noted that no effect was observed from the parenteral administration of lactose or galactose, which indicates that the site of action is probably the alimentary tract. It is possible, in view of this, that lactose may exert its effect through the development of acidophilic changes in the intestinal flora. However, this may not represent the actual or complete mechanism, as tetany was not found to be inhibited by the ingestion of dextrin which is known to produce acidophilic changes similar to those of lactose.

RAPHAEL, Ann Arbor, Mich.

BRAINS WITH TOTAL AND PARTIAL LACK OF CORPUS CALLOSUM; NATURE OF LONGITUDINAL COLLOSAL BUNDLE. C. DE LANGE, J. Nerv. & Ment. Dis. **62**:449, 1925.

A case of absence of corpus callosum is described in a boy who died at the fifth month without having gained weight though breast-fed. There was an extensive polygyria, the corpus callosum was absent and the olfactory nerves and bulb could not be found. The formix was present on both sides. The microscopic appearance of the brain is described, and the literature on absence of the corpus callosum is reviewed.

[ARCH. PATH.]

ON ATYPICAL AND MASKED FORMS OF ENCEPHALITIS EPIDEMICA (LETHARGICA) ON A BASIS OF ABOUT 125 CASES. AXEL V. NEEL, J. Nerv. & Ment. Dis. **63**:1-16 (Jan.) 1926.

Following seven years study of cerebrospinal fluids of patients on a neurological ward, the author is now aware of the fact that certain specific findings are occurring more frequently in these fluids than formerly, regardless of the patient's clinical diagnosis. A review of these clinical diagnoses and symptoms, which were other than encephalitis, now suggest encephalitis of some sort. Also there is now found a sharp increase in numbers of this type of patient coincident with the epidemic of lethargic encephalitis in 1919.

Various diagnoses had been given these patients. A great many symptoms are shown, masking the encephalitis, yet apparently due to lesions found in those parts of the brain in which epidemic encephalitis locates itself. Changes in these cerebrospinal fluids corresponding with findings expected in cases of inflammation, were more frequent during the years of the epidemic, and showed a tendency to decrease as epidemic encephalitis declined.

A tabulation of cerebrospinal fluid findings is given.

FLOYD, Iowa City.

PSYCHOLOGY AND SOCIAL HYGIENE. HUGH CRICHTON MILLER, J. Social Hyg. **12**:14 (Jan.) 1926.

In this address, delivered before the British Social Hygiene Council, Dr. Miller discusses the tendency to blame our present social laxity to "freedom." He feels that the solution is not to limit freedom in social conduct, but to use it for self-realization rather than self-annihilation. Purposeful self-restraint is not repression, and will not lead to the development of neuroses; the latter result from a refusal to recognize and face the issues involved. The whole question should be presented on a basis of progressive evolutionary idealism, if a dynamic code of ethics is to be developed. BOYD, Iowa City.

WHAT DO WE MEAN BY "NAUGHTINESS"? H. DOUGLAS SINGER, Wisconsin M. J. **25**:14 (Jan.) 1926.

Are we not still inclined to regard social misbehavior as "innate wickedness"? The reasons for the failure to learn control may result from defect or disease, or it may be the outcome of lack of training, or training that promotes delinquency. Society should not only punish the delinquent but should seek to prevent the delinquency, by seeing that the proper training is given.

The author gives several brief illustrations of faulty training, and concludes by saying that naughtiness is not an inherent quality but is the outcome of quite natural and essentially valuable longings and desires, which for some reason have not been subjected to the control of habits that are socially permissible. KASTNER, Milwaukee.

THE ANATOMIC BASIS OF DECEREBRATE RIGIDITY. N. ZYLBERLAST-ZAND, Rev. neurol. **1**:998 (June) 1925.

Having recalled the careful experiments of Rademaker which proved irrefutably that the red nucleus presides over the regulation of the normal tonus of the body, the author, on the basis of the experiments by Sherrington, Horsley, Magnus and Thiele which prove that the cerebellum is not the center of decerebrate rigidity, expresses the view that this center must be sought in the medulla oblongata below the level of entry of the eight cranial nerves. Transection of the brain stem at this level produces flaccidity of the rigid muscles almost every time. In an attempt to find the center for decerebrate rigidity, the author recalls the Hunter experiments which have shown that Deiter's nucleus has no influence on decerebrate rigidity. A method of injuring the olivary bodies is then described and the results of the experiments are reported. In two cases, section of the olive on one side led to disappearance of the rigidity on both sides. In another case, destruction of one olive was followed by flaccidity of the rigid muscles on the same side. The author calls attention to these results without making, however, any definite statement on the importance of the olivary formations in decerebrate rigidity.

CESSATION OF THE EPILEPTIC FIT AFTER INTRAVENOUS INJECTION OF CALCIUM CHLORIDE AND FAVORABLE RESULTS OF SUCH TREATMENT IN EPILEPSY. M. PETZETAKIS, Rev. neurol. **2**:174 (July) 1925.

The author reports two cases of essential epilepsy treated for several months by means of intravenous injections of calcium chloride. During the first month 0.5 Gm. was given each two days. In the second month the dose was raised

to 0.8 Gm., and in the third lowered again to 0.5 Gm. During the fourth month two injections of 0.8 Gm. were given weekly. The course in both cases was favorably influenced by this treatment. In the first case, when an injection was made during a seizure, the fit stopped after one minute, the ordinary duration of the attacks being from ten to fifteen minutes. Later, the calcium treatment led to disappearance of the fits which had usually appeared each month. In the second case, during the fourth month the patient, who usually had a monthly fit and two vertigo attacks, had only one short fit after the second month of treatment.

FERRARO, Washington, D. C.

EXPERIMENTAL AND PATHOLOGIC STUDIES ON PROGRESSIVE MUSCULAR ATROPHY. K. KURE, S. HATANO, T. SHINOSAKI and T. NAGANO, Ztschr. f. d. ges. exper. Med. **47**:77, 1925.

The authors' experimental and clinical studies indicate that progressive spinal muscular atrophy and amyotrophic lateral sclerosis are the result of degeneration of motor ganglion cells in the anterior horn of the spinal cord, while the sympathetic system is slightly involved or remains intact. Progressive muscular dystrophy is the result of disturbance of the autonomic system.

S. A. LEVINSON.

MENTAL DISORDERS DURING AND AFTER EPIDEMIC ENCEPHALITIS. V. MAKELA, Helsinski, 1923, 236 pages. Act. Soc. Med. Fennicae, "Duodecim," **4**, Pt. 2.

Twenty-one cases of epidemic encephalitis were investigated to decide whether the mental disorders occurring in the course of this disease are a clinical entity or are related to other psychoses. The variety of symptoms makes it difficulty to unify and trace them to a common etiology. In the beginning of the disease there is a peculiar depression with a general feeling of indisposition, but without localization of symptoms. There also are cases of pronounced mania with motor excitement. It is easy to differentiate them, however, from true manic excitement by the absence of euphoria and dissociation of ideas. This period is followed by one of delirium with disorientation as to time, place and persons. In 80 per cent of all cases hallucinations and illusions resembling those of delirium tremens are added; but in epidemic encephalitis the suggestibility is not so marked as in delirium tremens. The perceptive faculties are surprisingly well preserved, as may be demonstrated when the attention of the patients can be fixed during the tests. But there are marked disturbances in the ability to form and combine abstract concepts, which persist for a long time after the encephalitis subsides. A marked lack of memory for numbers and sentences, as well as for events and experiences of former years, was noticed. There was no marked disturbance of consciousness during the delirium and only in a few cases was the author able to detect amentia, which has been more frequently reported by other investigators.

These exogenous psychologic reactions are of minor importance in comparison with the disturbances of energy, emotions, impulses and will, the impairment of which is due to the difficulty of transforming will into action rather than to a lack of will or emotion. Catatonia like pictures were rarely seen. In schizophrenia the inhibition of muscular action is of psychic origin; in encephalitis it is due to disease of the extrapyramidal system. A depressve type of psychosis predominates. Frequently there are ideas of suicide. Irritability and whining are sometimes replaced by a peculiar indifference to the environment which may even amount to complete lack of emotion. There

may be a complete change in the personality. A young patient, normal at the onset of the encephalitis, may present the reactions of a psychopathic child. Attention is diminished without impairment of conception. The ability to form and combine abstract concepts may be well preserved, but with sudden disturbances in the logical sequence of ideas combined with flight of ideas and peculiar aberrations. Very seldom is there lasting impairment of memory, though this is sometimes simulated by fatigue with diminution of mental activity. Somnolence, first emphasized by Economo as characteristic, is not the typical symptom in epidemic encephalitis; the most striking feature is the shifting of sleep to the early hours of the morning and forenoon after preceding periods of unrest. The attempt to localize the lesion responsible for these symptoms was not successful. Cortical disturbances seem to be of minor importance compared to the lesions in the brain stem. There must be a certain constitutional disposition to produce the symptoms described. Susceptibility to exogenous toxic influences is not identical with the disposition for endogenous disturbances as is proved by the differences in behavior in epidemic encephalitis from that in well known endogenous psychoses. The conclusions of the author are based on extensive and carefully carried out psychologic tests. The psychic manifestations in epidemic encephalitis, as the author states, are as manifold as the individual dispositions of the patients.

WEIL, New York.

Diseases of the Ear, Nose and Throat

MASTOIDECTOMY: WITH SPECIAL ATTENTION TO LOCAL ANESTHESIA. S. M. BLACKSHEAR, New Orleans M. & S. J. **78**:137, 1925.

One half of 1 per cent solution of apothesine or procaine is injected into a wide area of skin, under the periosteum and into the posterior wall of the external canal. Satisfactory anesthesia has been obtained in several cases.

CONCLUSIONS FROM THE CORRELATION OF LABORATORY FINDINGS, CLINICAL SYMPTOMS AND END-RESULTS IN TONSILLECTOMY. L. S. LIPPINCOTT, New Orleans M. & S. J. **78**:395 (Dec.) 1925.

The author has attempted to correlate the gross appearance, microscopic appearance, bacterial flora, symptoms and the end-results of tonsillectomy and adenoidectomy. He concludes that there are no bacteriologic or morphologic findings typical of any given symptom, nor does any particular finding in the tonsils or adenoids serve as a means of prognosis of the end-results.

ANDERSON, New York.

METHOD OF INVASION OF POSTERIOR FOSSA IN OTITIS MEDIA. F. FREMEL, Monatschr. f. Ohrenh. **4**:400, 1925.

Three courses are generally recognized: (1) preformed route, wherein bony plate, meninges and brain cortex separate middle ear from brain abscess; (2) direct invasion of infection from middle ear through the structures before mentioned; the usual method, (3) metastasis through the blood circulation.

Körner calculates 42 per cent by the direct invasion. In forty cases of cerebellar abscess, there were two instances when the bone separating the middle ear from the abscess was normal in appearance. Hencke in twenty-four cases found three such instances. Blau collected 737 brain abscesses in literature, forty of which showed macroscopically no direct invasion of the brain.

The authors concluded, therefore, that the intracranial complication was metastatic. This cannot be inferred unless microscopic examination of the intervening bony wall and meninges is made.

Kümmel, Hinsberg, Miodowski and Karl Beck reported histologic studies, demonstrating the invasion of the cranium through preformed channels; in the case of cerebellar abscess the route is through the labyrinth, sigmoid sinus, posterior antral wall or the hiatus subarcuatus. The last named is a small dell on the posterior surface of the petrous bone, lateral to the internal auditory meatus near the apex of the pyramid. A process of the dura is firmly attached to this spot, which, though quite prominent in the child's skull, in the adult's becomes much shallower or even obliterated.

Fremel reports two cases of cerebellar abscess in which serial, microscopic study disclosed a direct, progressive invasion of the brain. Whether a meningitis or an abscess results after such an invasion depends apparently on the resistance of the dura (in addition to other factors, such as virulence of the organisms, duration of the middle ear suppuration). If the process reaches the dura and remains intradural for a time, permitting a firm adherence of the dura to both bone and brain cortex, further extension results in an abscess. Rapid extension through the dura does not afford the opportunity of dural adhesion and results thereby in a diffuse meningitis: GLOWACKI, Detroit.

Diseases of the Skin

ICHTHYOSIS AND CONGENITAL SYPHILIS. MARCEL SENDRAIL, Ann. de dermat. et syph. **6**:544 (Aug.-Sept.) 1925.

Citing nine cases from the literature, the author describes a case in which the ichthyosis is perhaps to be attributed to altered cutaneous development due to syphilitic infection *in utero*.

PITYRIASIS RUBRA PILARIS. H. GOUGEROT, Bull. Soc. franç. de dermat. et syph. **32**:374, 1925.

A girl, aged 5 years, was apparently in good general health, and her family history showed no sign of tuberculosis. An extensive eruption typical of pityriasis rubra pilaris clinically was cured following the injection of the antituberculous vaccine of Vaudremer.

SCLERODERMA AND SUBCUTANEOUS CALCAREOUS GRANULATIONS. THIBIERGE, L. SPILLMANN and WEISSENBACH, Bull. Soc. franç. de dermat. et syph. **32**:R.N.58, 1925.

In a girl, aged 14 years, the condition had appeared following an attack of diphtheria in 1916. It had progressed rapidly, and the arms and legs were extensively involved. Some of the nodules had broken through the overlying skin, as is shown by a photograph. PARKHURST, Toledo, Ohio.

PRIMARY FIBROSARCOMA OF THE SKIN IN A BOY 5 YEARS OLD. G. BERTACCINI, Arch. ital. dermat. e sifil. **1**:1 (July) 1925.

The patient suffered from a hard, pink, nodular lesion on the right knee over the rotula, which had been growing slowly for two years. No other lesions and no enlarged glands were found. The tumor was removed surgically, and there was no further reproduction. Pathologically the growth was a fibrosarcoma.

VEGETATING STAPHYLOID DERMATITIS. M. ARTOM, Gior. ital. di dermat. e sifil. **66**:1138 (Oct.) 1925.

The author reports a case of this condition in a child, aged 10. The lesions were situated on the face. *Staphylococcus pyogenes-albus* were isolated in pure culture from the vegetating masses. The author concludes from his bacteriologic and experimental studies that dermatitis staphylogenes is the result of infection with attenuated germs, which in a normal state of virulence would produce abscesses.

ZOSTER AND VARICELLA. C. MADERNA, Riforma med. **41**:1160 (Dec. 7) 1925.

The question of the identity of the specific germs of varicella and herpes zoster is still unsettled. Epidemics of herpes zoster coincident with epidemics of varicella have been reported, causing some observers to believe that possibly both diseases are produced by the same etiologic germ. This agent would produce a herpes zoster when infecting the nervous system and varicella when the infection is hematic. The author reports an epidemic of varicella and herpes zoster in the same family. He advises autohemotherapy in the treatment of herpes zoster.

PARDO-CASTELLO, Havana.

CONTRIBUTION AND INQUIRY INTO THE RELATION OF ERYTHEMA NODOSUM TO TUBERCULOSIS. A. BREMS, Ugesk. f. Læger **46**:1008, 1925.

Four cases of erythema nodosum are reported, in which positive diagnoses of tuberculosis is the most important etiologic factor of erythema nodosum.

SCHLUTZ, Minneapolis.

A CASE OF "PINK DISEASE" (ACRODYMIA, ERYTHREDEMA, ERYTHÈME ÉPIDÉMIQUE). S. M. C. VAN VEEN, Geneesk. Gids. **3**:1153, 1925.

A case report is given of a child, who when 4 months old presented symptoms of pink disease for the first time, marked muscular hypotonia, intense perspiration and dulness. Anorexia and photophobia also developed. In the beginning of the disease the pseudoparetic condition was often changed into one of general spasm, lasting only some minutes. This singular symptom disappeared gradually, and after 8 weeks it was no longer observed. The characteristic symptoms on fingers and toes in this disease (bright red, swollen and moist skin, desquamating later on) did not become obvious until some weeks after entrance to the hospital. An eczema lasting from before the beginning of this disease became more intense. During the illness the child developed angina, pyelitis and some skin abscesses. The pulse was small and frequent. The spinal fluid showed no abnormalities. The blood picture in the beginning was normal; during the pyelitis, 16,000 leukocytes with a severe deviation to the left was noted (Schilling symptom).

No explanation could be found for the photophobia which disappeared afterward. After several months the child recovered slowly, the muscular tonus at the time of the publication of this case was however still very slow.

VAN CREVELD, Amsterdam.

Surgery and Orthopedics

SOME INDICATIONS FOR SPLENECTOMY. JOHN B. DEAVER, M. J. & Rec. **122**:641 (Dec. 2) 1925.

The author first enumerates the various hypotheses offered with regard to the functions of the spleen. He then gives the immediate effect of splenectomy,

pointing out that one of the ways of studying the functions of an organ is to observe the effects of removal of the organ in question. Physiologically, splenectomy produces certain changes in the blood which cause a temporary anemia, an increased resistance of the red blood cells to hemolysis and a reduced tendency to jaundice. Splenectomy also causes an increased excretion of iron, decrease of fat in the feces, an increase of fat and cholesterin in the blood. This last mentioned may aid the resistance of the red cells to hemolytic agents. Any splenic tissue left after operation rapidly increases in size, becoming equivalent to a normal spleen in size and appearance.

This brief outline of some of the changes that follow splenectomy explains the result of the operation per se. Splenectomy gives the best results in pernicious anemia when performed in the early stages. In acquired hemolytic jaundice and the splenic anemias, the operation is one of distinct value. In Banti's disease and the thrombocytopenic type of purpura hemorrhagica splenectomy is also of value. The author gives the operation in detail, pointing out its difficulties. It is not simple but is a serious procedure. The greatest dangers after the operation, aside from shock and collapse from hemorrhage, are bronchitis and pneumonia. A late complication to be feared is intestinal obstruction from adhesions. The remote results of splenectomy are, on the whole, excellent.

WILLIAMSON, New Orleans.

PRIMARY SARCOMA OF THE INTESTINES. FRANK L. LORIA, New Orleans M. & S. J. **78**:201, 1925.

The author presents a case of primary sarcoma (lymphosarcoma) of the descending colon in a boy, aged 3 years. The insidiousness of the onset, the relation of trauma as a possible etiologic factor and the rarity of the location of the tumor are emphasized.

The author also summarizes the cases previously reported in the literature.

THE ROENTGEN RAY IN OSTEOMYELITIS. LESTER J. WILLIAMS, New Orleans M. & S. J. **78**:267, 1925.

The author emphasizes the importance of roentgen-ray examination in early osteomyelitis. The chief diagnostic value lies in the exclusion of other pathologic conditions which may be confounded with osteomyelitis.

ANDERSON, New York.

Miscellaneous

THE EFFECT OF THYRO-PARATHYROIDECTOMY AND PARATHYROIDECTOMY AT 75 DAYS OF AGE ON THE GROWTH OF THE BRAIN AND SPINAL CORD OF MALE AND FEMALE ALBINO RATS. FREDERICK S. HAMMETT, J. Comp. Neurol. **37**:15 (June) 1924.

This paper is one of a series (No. XX) reporting the investigation of the rôle of the thyroid apparatus in the growth of the central nervous system from the point of view of age and sex relationships.

It contains the observations and discussion of the effects of the lack of thyroid and parathyroid secretion on the growth and differentiation (water solids) of the brain and spinal cord of male and female albino rats, during the age period from 75 to 150 days, together with a comparison of the data of similar observations on control rats observed during the growth period from 100 to 150 days of age.

The author comes to the following general conclusions:

1. Sex and age are factors of importance in the determination of the type and degree of response in growth of the brain and cord to thyroid and parathyroid deficiency.

2. The brain is more dependent on thyroid function for its normal quantitative differentiation than is the cord. This difference is interpreted primarily on the basis of the relative time of appearance of the spinal cord, thyroid gland, and brain (cerebral hemispheres) during the course of phylogenetic evolution. It is secondarily interpreted by the differences in relative dependence of cytoplasmic and lipoid metabolism on thyroid function.

3. The growth of the central nervous system is more resistant to the toxemia of parathyroid deficiency than is that of the body as a whole.

4. The growth of the spinal cord is more resistant to the disturbances of metabolism induced by thyroid and parathyroid deficiency than is that of the body as a whole.

THE SIGNIFICANCE OF THE FRONTAL BRAIN WITH RESPECT TO THE HIGHER PSYCHIC FUNCTIONS. JULIUS DONATH, J. Nerv. & Ment. Dis. **61**:113 (Feb.) 1925.

A. Motor Centers of the Frontal Brain:

The opponents of the localization of the higher psychic functions in the frontal brain admit motor functions only:

(1) The motor center of speech (Broca's area). This is localized in the posterior third of the left third frontal convolution. According to Mingazzini, the verbal impulses proceed from the right Broca's area, traversing the anterior part of the corpus callosum, and uniting with the left side.

(2) Fronto-ponto-cerebellar tract serving equilibratory functions. Flechsig locates it in the third, and Brodmann in the first and second convolutions. Some authors, as Gerstmann and Monrad-Krohn, deem it an equilibrium center superordinated to the cerebellum, exercising a consciously regulating influence on the opposite cerebellar hemisphere, while the latter is unconsciously exercising its equilibrating activity. Bruns has emphasized "frontal ataxia," and Bárány showed that frontal tumors can cause cerebellar as well as vestibular symptoms.

(3) Projection fibers from the convexity of the prefrontal region (from the second and third and partly from the first convolution) within the area of the corona radiata in the anterior crus of the internal capsule to the basal ganglia.

(4) Association fibers which unite the cotex of the frontal brain with other parts of the cortex, especially the fasciculus arcuatus or fasciculus longitudinalis superior, from the second and third frontal convolutions, partly sagittal to the occipital lobe and partly in arcuate form to the vertex of the temporal lobe.

(5) Monakow's frontocentral fasciculus, from the frontal brain to the anterior central convolution.

(6) The graphic and motor-musical centers, with uncertain localization. Both are placed in the second frontal convolution—the graphic in the left, and the motor-musical sometimes in the right, especially in the foot of the convolution. It is noteworthy that they border immediately on the center, for the movement of the hand and fingers in the middle of the anterior central convolution similarly to the center of speech bordering on those of the tongue, gullet, jaw and larynx in the foot of the central convolution. The sensory-musical center was placed by Probst in the foremost part of the first left temporal convolution.

Pick, Wernicke and others assign the graphic center to the medulla of the lower parietal lobe corresponding to the angular gyrus. Evidently the visual tracts passing underneath to the occipital lobe are affected by lesions here, and the integrity of these tracts is indispensable to the mediation of letter images to the center of the hand and finger movements. Mingazzini's view is, however, that lesions of the inferior parietal lobe, and especially of the left angular gyrus, are connected with disturbances of reading, which are independent of aphasic syndromes.

While agraphia is usually found in lesions of the second left frontal convolution, motor amnesia is encountered on both sides, which may be attributed to the use of both hands in playing on musical instruments.

Thus it seems that engrammes (images) are deposited in the frontal brain which, together with the impulses of the will also enacted here, move the motor centers. In Broca's center, the speech-moving images set in motion the bordering centers of the necessary muscles in the anterior central convolution. From the graphic and musical center in the second frontal convolution the impulses are converged to the neighboring hand and finger centers. The recollection of images, the ideas, as well as their comparison with each other, and the assertion in judgment, the pondering of actions and decisions to carry them into effect, occur in the frontal brain, and then follow the impulse to the muscle centers. Beginning from the cortex of the central convolution, the movement is purely mechanical. Thus the frontal brain seems to be physically superordinated to the motor centers of the anterior centrol convolution.

B. The Higher Psychic Functions of the Frontal Brain:

Here are first recorded numerous instances of frontal lobe lesions, mostly tumors, which emphasize the lack of psychic findings. However, in such cases the author feels that in the great majority of these cases, if attention had been called to them, a closer examination would have shown psychic changes or defects.

C. Focal Diseases of the Frontal Brain, in the Form of Progressive Paralysis, Schizophrenia and High-Grade Dementia:

(1) Forms similar to paralysis:

Bernhardt and Borchardt, Sullivan, Van Gehuchten, Witney and Rosenback have all reported cases which, as syndromes almost similar to general paralysis developed, have, either at operation or necropsy, proven to be tumor formations involving the frontal lobes.

(2) Forms Similar to Schizophrenia.

Mr. Rosenfelt reports the case of a rifleman, aged 20, who was shot through both frontal lobes by an infantry projectile. A psychic disturbance of two months' duration supervened, so much like catatonic stupor that "anyone not knowing the history of the condition would have, without hesitation, pronounced it a catatonic stupor." This patient also showed "frontal ataxia." There was complete recovery in three months. E. Forster, in a case of similar injury, observed no defect of intelligence in the restricted sense, but a lack of impulse with cataleptic symptoms. Schob, in a third similar case, saw, as a permanent condition, impaired memory, disproportionate decrease of intelligence, dulness, lack of intuition, euphoria, moderate irritability, impulsive running away and thoughtless actions. Dimitz and Schilder, in a case of tumor of the septum pellucidum growing into the corpus callosum, found loss of initiative, agility and interest, as well as disturbances of equilibrium and trembling fits. Bostroem, in four observations of frontal brain tumors, besides trunk ataxia and somnolence, emphasizes lack of activity and stubborn perservance in attitudes.

(3) Forms of High Grade Dementia.

Curti, in a case of neoplasm of the anterior fossa, observed, besides general tumor symptoms, disturbances of the sense of smell, marked weakness of memory, states of severe irritation, and idiocy. Constantini saw unconsciousness supervene after jaundice and later spastic paralysis and dementia in a case of tumor of the centrum ovale of the prefrontal lobe, proved postmortem. K. Mendel mentions three cases of severe frontal brain injury with remarkable jesting and euphoria. H. Richter reports a clear case of idiocy resulting from an isolated lesion of the ganglion cells in the frontal brain. Gans reports two somewhat similar cases, both in women, one aged 54, the other 61, who gradually developed a severe grade of dementia. Both showed marked frontal lobe atrophy. In a case of heredosyphilitic disease of the anterior cerebral artery and the left branch of the Sylvian artery, Düring saw right spastic atrophic hemiplegia, anesthesia and idiocy. In a case of sarcoma of the anterior part of the right cerebral hemisphere, Arvedo observed psychic disorders simulating hysterical symptoms: great suggestibility, violent fluctuations of the affections and temporary epileptiform attacks. Marie and Benoist, in a case of pure senile dementia, without motor, sensible and sensory disturbances, found a tumor under both frontal lobes.

D. The Corpus Callosum:

By means of the ample connections which it establishes between both frontal lobes, it forms an integral part of the frontal brain, so that lesions of the corpus callosum on the whole cause the same symptoms as those of the frontal brain. Because the tracts are pressed so closely together, small lesions may cause most extensive disturbances. Pagot asserts that the corpus callosum is the organ of the highest mental functions. Landsberger reported a case of an undeveloped state of the corpus callosum with serious psychic and somatic phenomena. Hultkrantz examined a brain without the corpus callosum. There had been no serious motor or intellectual defects, and he produced a dozen more similar reports from the literature. His explanation is that in such cases, one hemisphere alone undertakes the incitement and more subtle regulation of all spontaneous movements and that amnestic-associative functions are also confined to the same hemisphere, while the other half remains ineffective.

The significance of lesions of the corpus callosum in producing psychic disturbances becomes evident by the fact that here both frontal lobes are simultaneously indirectly affected to a great extent. The statistics of H. di Gaspero show that psychic disturbances occur more frequently in tumors of the corpus callosum than in frontal tumors. The occiptal, temporal and parietal tumors follow in order. Cerebellar tumors range from 30 to 40 per cent and the pituitary up to 20 per cent. Tumors of the brain stem and central territories are least frequent.

Moria (joking) is most common in frontal tumors; stupor in tumors of the anterior part of the brain; while melancholia, crepuscular states, hallucinosis and paranoia are not connected either with definite parts of the brain or with particular kinds of tumors. The findings show also an enhanced importance of the left hemisphere over the right.

E. The Clinically Ascertained Psychic Functions of the Brain:

From the type of psychic disturbances the author deduces the functions of the frontal brain. There have been found disturbances of memory and perceptibility, retrograde amnesia, confabulation up to complete loss of memory, as well as disturbances of conception, of the association of ideas and intuition, and weakmindedness up to idiocy.

Chorosko, from observations in fifteen war cases, asserts that in exclusive lesions of the left frontal lobe psychic disturbances had never been observed—which is contrary to Rauschburg's findings—that they are found in bilateral lesions only, or in those of the medial line. He assumes typical psychic disorders to be weakness of the attention manifesting itself in the decrease of the capacity of observation, of the stability and capacity of attention, as well as in irrational actions and in abnormal conduct generally.

Goldstein finds in frontal brain lesions psychic disorders of a subtle kind, characterized by a lack of capacity to discern the essentials of an event. From this disturbance arise inattention, lack of interest and power of concentration, symptoms in the domain of agnostic and apractic disorders, and lastly, akinesis.

In the frontal brain are thus deposited the engrams of things and events. There they are compared with each other, abstracted to ideas, connected to judgments and concluding verdicts formed. There the action is weighed and the impulse of the will imparted and from the sphere of ideas converged to the proper motor centers, where the purely psychic act of the frontal brain is transformed by reversing in movement. The impulse of the will does not arise in the cortex of the central convolution, but in the frontal brain, and only comes into activity through reversing.

It is noteworthy from the results of the World War that persons with frontal brain injuries show greater mental defect than those with lesions of the central convolutions. From the measurements of the head by Bayerthal it is concluded that the size of the anterior part of the head is of importance for the mental faculties.

F. Experiments on Animals and Comparative Anatomy:

Franz observed that the extirpation of the left frontal lobe in the ape resulted in psychic deficiency, which was not observed on extirpation of the right lobe. Bianchi found one-sided extirpation in the ape produced no effect, but bilateral extirpation resulted in a diminution of the higher psychic functions. Franz, after teaching cats and apes certain tricks, extirpated their frontal lobes and found that they could no longer do the tricks. However, they recovered the ability by renewed drill. He thinks, therefore, that the frontal brain serves for learning and acquiring new associations, while the associations already formed are preserved in other parts of the brain. The author suggests this as proof for the vicariation of nerve cells and tracts. Ceni, by extirpation, ascertained that the maternal instinct in birds is dependent on the forebrain. Brodmann divides the frontal lobe histologically into a precentral region, representing the center of the arbitrary movements and a frontal region whose function, in his opinion, is unknown. The precentral region is present in all mammals, and its extent varies only within narrow limits. The frontal region is inconstant, being present only in the more highly organized animals as a special structure formation. It is most strongly developed in the anthropoids. Its surface in man amounts to 29 per cent of the whole brain surface; in the chimpanzee, to 16.9 per cent; in the gibbon, to 11.3 per cent; in two baboons, to 10.1 and 9.5 per cent, respectively; in *Cebus capucinus,* to 9.2 per cent; in the lemur, to 8.3 per cent; in the dog, to 6.9 per cent; in the cat, to 3.4 per cent; and in the rabbit, to 2.2 per cent. Flechsig, on the basis of his myelogenic findings, considers the frontal terminal area in anthropoids much smaller than in man.

The author, in his concluding remarks, speaks, not in favor of the exclusive, but only of the prevailing psychic, significance of the frontal brain. He does not deny the importance of the other association areas, but claims that the seat of the highest mental activity lies in the frontal brain.

AUGUST, Detroit.

Social Hygiene and the National Association. Edward L. Keyes, J. Social Hyg. **11**:513 (Dec.) 1925.

A survey of progress since the organization of the American Social Hygiene Association in 1914 reveals development of widespread interest in the problems with which the society deals. In this country there are now over 800 public clinics for venereal disease in operation. The policy of repression of prostitution has become quite general. An effort to improve the social environment is designed to protect the youth, and to prevent delinquency. Sex education is receiving the attention it merits. There is unity of purpose in both hemispheres in policy and activities pertaining to social hygiene.

Some Social Hygiene Observations in Europe. Rachelle Yarros, J. Social Hyg. **11**:535 (Dec.) 1925.

Summarizing her observations made during visits to European venereal clinics, the writer comments on the prevalence of good clinics, and their large patronage. Public sentiment is becoming opposed to the reglementation of prostitutes, and in France, Germany, Russia and England many agencies are employed in the rehabilitation of sex offenders. The police clinics, in contrast, are far from desirable.

Guarding the Nation's Health. Hugh S. Cummings, J. Social Hyg. **12**:25 (Jan.) 1926.

In an address dealing with venereal disease control, the activities of the Federal Public Health Service are outlined and discussed. Educational and legal phases are given most consideration.

Boyd, Iowa City.

Cocaine Addiction in Child. Cunha Lopes, A Folha med., p. 12, Jan. 1, 1926.

The *Folha Medica* of Rio de Janeiro cites a case recently reported by Dr. Cunha Lopes in which a girl, aged 13, employed in a dentist's office, had become a cocaine addict, swallowing the drug. Hallucinations and attempts at suicide, with loss of memory and 8 per cent of urea in the blood, were the main features of the case.

Cushing, Chicago.

Proceedings of the Thirty-Sixth Congress of the German Society for the Study of Children's Diseases, Karlsbad, 1925. Monatschr. f. Kinderh. **31**:193, 1925 and 1926.

The German Pediatrics Society held its annual meeting for 1925 in a three days' session at Karlsbad. Abstracts of all the papers appear in a large issue of the *Monatschrift*, covering about three hundred pages. The general average of the studies reported is unquestionably superior to that of the few years preceding. Readers who know the Germany of a decade ago will be interested in noting the increasing number of quotations from the American literature.

On the first day, Hans Spitzy of Vienna presented a long essay covering the borderline of pediatrics and orthopedics. He devoted considerable time to the subject of clubfoot and urged its early treatment. True clubfoot is a congenital defect occurring in several generations. It should be corrected as soon as the period of icterus neonatorum has passed. Before this, the skin is too sensitive to the pressure of any bandage or cast. Congenital torticollis, too, should be operated on in the first weeks and the operation of choice is the

open one. Flat feet in children should not be strapped or subjected to the various appliances so frequently used. The problem is one of educating the muscles, and here Spitzy suggests what seems an ingenious device. He puts a button in the sole of the child's shoe, and instructs him to walk so as not to disturb it. The period is prolonged from a few minutes to a half day, and during this time the proper muscles become strengthened. For scoliosis not so much can be accomplished. Here prophylaxis assumes the position of greatest importance. He urgently recommends that school periods be limited to four hours daily and that these be interrupted at frequent intervals. The future of orthopedics, like that of pediatrics, will be in preventive work. Children at school should have a prescribed course in physical exercises as well as in the usual curriculum. As regards tuberculosis, he warns that sunlight alone will not cure all cases. Fresh air and food are equal necessities. Often prolonged exposure to the sun's rays destroys the appetite and defeats the whole treatment.

Other speakers were Friedrich Holtz, who presented a method for the determination of blood phosphorus which required only a few drops of blood. Bischoff investigated the length of time it takes sodium hydroxide to lake blood, and found it varies during different months of infancy. He tabulated his findings and presented them as a method of determining the age of a child when no history is obtainable. A. Uffenheimer made a number of skin tests on patients with bronchial asthma and found the method of value. Eckstein of Dusseldorf argued that metabolism tests taken during the usual short period of time are worthless and should only be used relatively. In the goiter of adolescence, he found no change in the metabolism. The fact that the thyroid can tolerate large doses of iodine, and that in these cases only tiny amounts work a cure, lead him to suggest that for such cases iodine may function simply as a catalyzer and not as a replacement of some deficiency. Fritz Demuth of Marburg found that extracts of different organs vary in their ability to split a certain phosphorus compound. Otto Beck of Tubingen, and A. Frank of Leipzig contributed short studies on the metabolism of fever and on fat metabolism in hunger.

A number of papers and considerable discussion centered on the measles question, with reference to the organisms found by Caronia and to his method of prophylaxis. The majority of speakers could not confirm his optimistic reports, though some thought that inoculations of a vaccine of his organisms had some slight prophylactic value.

Samet and Tazner of Vienna found that in the child, digitalis affects both the normal heart and the heart in pneumonia in the same way. They cannot confirm the American observations that digitalis invariably causes a diminution of the "T" wave. In small children, the dose of 0.2 gram of the powder in 24 hours should not be exceeded.

Koreff and Hans Mautner reported studies of the action of insulin and pituitary extract on the gastro-intestinal tract of mice. Insulin seems to tone up the musculature and increase secretion, while pituitary extract has the opposite effect.

During the second day, much of the time was given to the discussion of blood transfusion. In this respect, the Europeans do not seem to have as great experience as we have, and are now going through the various stages in the development of the subject that we have gone through during the last decade. Pyloric stenosis also came in for its share. The consensus of opinion is that most patients recover without operation. When to operate was the subject of some debate. J. Bauer of Hamburg advised surgery when the stomach has

not emptied any of a bismuth meal after two hours. Herman Vollmer showed that in severe pyloric stenosis the loss of acid from vomiting lead to a relative increase of alkali. That so few of these patients developed tetany is an argument against alkalosis as an etiologic factor in that condition.

Von Bokay of Budapest intubates children under 2 years of age, and urges early interference. The discussion between him and Schlossman of Dusseldorf was somewhat acrimonious, Schlossman claiming that if one desires to advertise a mortality of 50 per cent as a good result, the interpretation is one determined by the listener's temperament. Schick acted as peacemaker. Biedl read a long complicated paper on the endocrine changes at puberty. Franz Hamburger (Graz) presented studies, showing that individuals both react differently and possess varying amounts of antibodies on different days.

The end of the day's program and much of the third day was taken up by studies of nutrition. Rosenbaum (Leipzig) reported an interesting research on dogs, and concluded that no matter what the nature of the food, the reaction of the duodenal contents was maintained constant. Thus, acid foods, such as albumin milk, would work a much greater stimulus on the duodenal mucosa that those of a less acid nature.

Considerable discussion was aroused by K. Weise (Leipzig), who attempted to repeat the observations of Adam that different strains of colon bacilli vary in their ability to ferment carbohydrate. He was unable to change one type of bacillus to the other until he injected a culture into the peritoneal cavity of a guinea-pig and passed the organism through several animal inoculations. By this procedure the carbohydrate fermenting power of the organism was greatly increased. Hofmeier also reminded us that organisms of the same type varied, and that we must always bear in mind different characteristics of a various strains.

Eugene Stransky of Vienna and Alfons Trias of Barcelona presented a good study of the intestinal bacteria of the dog. Three animals were fed naturally and four artificially. Cultures were taken from various levels of the gastro-intestinal tract. In the stomach and upper intestine, bacteria of the same type were found in both series of animals, being more numerous, however, in the artificially fed. In the lower ileum, differences become manifest. While in the naturally fed the organisms are of the bacillary type and seem homogeneous, in the artificially fed there is no distinct type of organism, and extraneous forms such as yeasts become common. Studies were also made on the proteolytic activity of the organisms. The aerobes acted identically in both series of animals. The anaerobes seemed more active proteolytically in the naturally fed.

Hugo Meyer (Freiburg) gave chemical evidence to show that human casein is not an absolute constant, but that there is variation in some of the reactions of different specimens of breast milk. Ernst Maurer (Munich) produced rickets in rats, and found an unquestionable change in the blood. There was an increase of the nucleated reds and an increase in eosinophils and myelocytes.

The session closed with some brief clinical observations on syphilis, and with an experimental study on tuberculosis by Berthold Epstein of Prague, who showed the incubation of that disease in animals to be from three to ten weeks. This period is entirely without symptoms and can be demonstrated only by tuberculin reactions.

GERSTLEY, Chicago.

Society Transactions

CENTRAL STATES PEDIATRIC SOCIETY

Third Session, Chicago, Nov. 7, 1925

JOSEPH BRENNEMAN, M.D., *President, in the Chair*

SKULL FRACTURES. Presented by DR. ALBERT H. MONTGOMERY.

In the last five years we have seen forty-two cases of skull fracture, all intimately associated with intracranial injuries. In this series none of the patients were new-born infants, but ranged in age from 4 months to 14 years. In thirty-four of the cases the injury was located in the vault alone, and in the base alone, or associated with the vault, in the remaining eight cases. The linear fractures of the vault are of little interest beyond the point at which they may touch important blood vessels or important nerves. The fractures of the base are frequently associated with the orifices of the head, and are apt to give entrance of infection to meninges. The depressed fractures are extremely important, for they call for some type of immediate active interference. In our series, twenty-seven of the fractures were simple, unassociated with wounds of any type.

One of the most important symptoms associated with injury to the skull is that of temperature. This usually rises and those that reach 103 or 104 F. indicate a definite injury to the brain. A subnormal temperature is also indicative of severe injury. The pulse is generally slow, but this does not indicate cerebral compression unless it occurs with other signs and symptoms. The urine often contains albumin and casts, and lesions about the hypophysis are habitually associated with the presence of a sugar reaction in the urine. Spinal puncture gives valuable information.

In the treatment we have a simple working rule that we have followed after a certain amount of disaster in these cases. In the depressed fractures we operate as soon as possible, only waiting for a certain degree of shock and concussion to subside. This holds true of the perforated fractures as well. The other group of cases that we feel demand operative attention are those that show compression. Localized symptoms associated with hemorrhage, or definite cerebral edema, with intracranial tension that persists after twenty-four hours, are the big indications for surgical intervention. All other cases of fracture of the skull are treated by conservative measures such as ice bags, sedatives and rest in bed, with attention to the bowel and bladder.

CARDIOSPASM? Presented by DR. W. H. O. HOFFMANN.

CASE 1.—The patient was the third child in the family. The first child had congenital coloboma of both eyes, otherwise was apparently normal. The second was a mongolion idiot with a congenital heart, who died at the age of 2 months. The child in question was seen on Sept. 21, 1925, the fourth day after birth, with the complaint of vomiting. He vomited during every feeding, never after feeding. While he was nursing he would let the nipple go after three or four swallows and the food would run out of his mouth. He would start to nurse over and

over again, each time with the same result. He had lost from 7 pounds, 8 ounces, to 6 pounds, 11 ounces, had a sighing respiration, slight cyanosis, and the skin felt very dry. On fluoroscopic examination the barium would go readily down to the end of the esophagus, but no further. The esophagus seemed to be rather wide. The stomach tube, after several minutes, entered the stomach. For five days thereafter, the feeding was done by tube, using as large a tube as possible. Gradually, the child was put to the breast on alternating feedings and finally the tube was omitted. The child is now in good condition. This may have been a cardiospasm, or some mild stenosis of the cardia.

CASE 2.—This patient was the first child in the family, and was seen on the third day. He acted at the breast similar to the before mentioned child, and, in addition, would vomit large quantities later. On the fourth day of life, under the fluoroscope, a picture similar to that of the first baby was seen; that is, the barium would go down to the cardia and would remain there from twenty to thirty seconds. At intervals, after the whole esophagus was well filled, barium entered the stomach. A roentgenogram, taken three hours later, showed a large amount of the barium still in the esophagus, the lower end of the barium shadow ending in a small fine tip. A roentgenogram, taken twenty-four hours after, showed a liberal amount of barium still in the stomach. The child was fed with the tube the same as in the previous case, and was given atropine before each feeding. Occasionally, there were large quantities vomited. Today the child is in good condition. He probably had a cardiospasm plus a temporary pylorospasm.

CONGENITAL DEFORMITIES. Presented by DR. E. J. BERKHEISER.

In this small group of patients, we have to deal with congenital deformities which have restriction of motion in the joints. No definite etiologic factor is known. Pathologically, we find that the principal loss of motion is that of extension. This is due to a thickening of the joint capsule and all the periarticular structures. All of the soft parts, as well as the tendons, have structurally shortened or adapted themselves to the flexed position, and in one of the cases there is a congenital bony ankylosis of the knees in flexion. The thighs are big and "ham like" in appearance and the buttocks are broad.

This first child was brought for examination when about 1½ years of age with flexion deformities at the hip and knees, and clubfeet. In the first 18 months of life she had been operated on with sufficient force to tear the skin and soft structures behind the knees, and yet without correction of the deformities.

The second patient was similar, but with flexion deformities in the upper extremities. He has had his deformities corrected and now is able to stand erect and walk unassisted.

The third child was brought in with flexion at the knees and bony ankylosis. She walked on her buttocks by swinging her body from side to side. Osteotomies were performed on both knees, and now she walks on her feet with stiff straight knees.

The treatment is twofold. If there is bony ankylosis, an osteotomy must be performed. Otherwise, the tendons may have to be tenotomized. The long plaster double spica in the first case shows the method of treatment. However, the essential form of treatment is that of constant application of pressure by repeated change of casts until the deformities are overcome and then the deformities will not recur even in later life.

MADELUNG'S WRIST. Presented by DR. B. H. MOORE.

This is an unusual condition, that is known as "Madelung's wrist deformity." It occurs invariably in children of 12 or 13 years of age at the period of rapid growth. This is the third case we have seen. The signs are very slight in the beginning. There is usually pain in the wrist, which is diagnosed as "rheumatism," "growing pain" or "sprain." In a year or two, as the child grows, a curving of the radius is noted which is sometimes associated with a backward dislocation of the ulna. This is a marked case, showing the characteristic deformity with the ulna dislocated backward, the wrist being turned in. There is also some shortening of the forearm, and the condition is bilateral. In the roentgenogram there is a small, triangular area of lessened bone density on the head of the radius that is quite typical of these cases. This patient has been operated on, with considerable improvement in the hand, and she has good use of her fingers.

The operation consists in an osteotomy, taking out a wedge of bone sufficient to allow us to bring the hand back into the normal position.

As to etiology, I think that, at sometime during the period of growth, there has been a slight infection or slight trauma which has injured a portion, but not the whole of the epiphyseal end of the radius, so that the growth of this injured portion is delayed, but the rest of the epiphysis grows at the normal rate, thus causing the curvature.

POSTENCEPHALITIC CONDITIONS IN CHILDREN. Presented by DR. BERT I. BEVERLY.

Previous to 1918, encephalitis in children was a comparatively rare and unknown disease. Since the epidemic, however, the number of cases is apparently increasing. The number admitted to the Children's Memorial Hospital during the last two years is greater than the number admitted during the two years of the epidemic. From clinical and pathologic standpoints, both the acute conditions and sequelae may be divided into two large groups; namely, the infectious or epidemic group, and the toxic group. The epidemic subjects have acute symptoms, which have been carefully described by many writers, and characteristic histologic findings in the midbrain with slight changes throughout the brain. The sequelae of this group may be divided into those characterized chiefly by the development of a parkinsonian syndrome and those in which personality changes predominate. In the latter, the subjects are characterized by marked emotional instability, resulting in severe behavior disturbances without deterioration of intelligence as shown by mental tests. The outstanding clinical manifestations of the toxic cases are convulsions, rapidly developing and changing neurologic findings and general toxic condition of the patient. The onset may manifest itself at the beginning or late in the course of the infections. It is apparently always, or nearly always, secondary to an acute infection elsewhere in the body, usually of the upper respiratory or gastro-intestinal tracts. The cerebral symptoms may be slight, or sufficiently severe to cause early death. The histologic findings are characterized by changes in the pyramidal cells and throughout the cortex, with slight or no changes in the midbrain. One outstanding characteristic of this group is the marked deterioration of intelligence during the acute illness, and mental arrest as a sequel in some cases.

Cases were presented illustrating postencephalitic behavior disturbance, parkinsonian syndrome, cerebellar encephalitis, with complete recovery, respiratory difficulty, hemiplegia, following hemorrhagic encephalitis, convulsions with encephalitis as a probable factor and toxic encephalitis resulting in idiocy.

CELIAC DISEASE. Presented by DR. L. W. SAUER.

Up to 1921, I had poor results with my patients with chronic intestinal indigestion. At that time, Dr. John Howland reported excellent results with standard protein milk in thirty cases. About then I had a patient who was not progressing, and tried powdered protein milk. The child took the food fairly well after a week, and has gained ever since without exacerbations. At the time of writing he is over 5 years old and overweight. Up to this time, I have used this method of treatment in eleven cases of celiac disease, with striking results in most instances. In place of using the standard strength, I use a paste prepared of the powdered protein milk and water or Ringer's solution sweetened with saccharine. At times, vanilla is added so that the mixtures resembles ice cream. It is fed by spoon four times a day. The temperature of the water should be just 100 F. It is sometimes advisable to wash the food down with a teaspoonful of water after every few of food. We use as many tablespoonfuls of the powder in twenty-four hours as the child weighs pounds, and then gradually increase the quantity until the number of spoonfuls equals the average weight for that age. After the child has gained a number of pounds the second phase of the diet is begun: namely, the cautious addition of cottage cheese, lean meat, egg yolk, etc. After a few more weeks or months of progress, vegetable, zwieback, rice flour and sugars are cautiously added. The diet must vary according to the tolerance of the individual child. One child gained 14 pounds in twelve weeks; another did poorly because he had bronchitis and fever on admission, when this cleared up he made very rapid gains; two gained 14 pounds in six months; three others gained about 10 pounds in six months; two gained 9 pounds in six months. My last patient, aged 2¾ years on admission, had made no gain for practically a year. She weighed 20 pounds and 10 ounces. She was put to bed in the hospital, and during the first fifty days of an exclusively protein milk diet gained 134 ounces. All of my patients are still getting some protein milk; in none has there been an exacerbation. In five, the abdomens are still rather prominent, but the weights are equal or above that of the average child of that age.

PAROXYSMAL TACHYCARDIA. Presented by DR. HAROLD A. BACHMAN.

CASE 1.—The patient, a girl, aged 11 years, came to my clinic two years prior to the time of writing, with a history of rapid heart beat, dating back to the age of 6 years. During the first years, the attacks occurred once or twice a year, but, as she grew older, they became more frequent until they appeared once a month. She was admitted to the ward, and during the first few weeks had typical attacks which came on suddenly and ended suddenly, sometimes two or three times a week, and extended over twelve to twenty-four hours. Physical examination revealed no cardiac pathology. The tonsils were large, cryptic and infected. In the ninth week of her stay the tonsils were removed under local anesthesia. On the day of the tonsillectomy an attack of tachycardia began which continued for eight days. The pulse rate was over 200 by electrocardiographic count. During this entire period her heart did not dilate, she had no dyspnea and no edema. On the eighth day her pulse gradually became slower, and in two or three days it had returned to normal. After three weeks she had another attack of tachycardia lasting a few hours. She was in the hospital for two more weeks and then went home, where she remained for three months with only two short attacks lasting for a few hours. I felt that the tonsillectomy had been of some therapeutic value. Three months later she came in with a severe attack following an acute sore throat, remained in the hospital for two weeks and went home. A month later she was admitted again

with another acute attack following a cold. In the year and a half since her last admission, she has continued to have occasional attacks of tachycardia, and the mother states that during the last few weeks she has had two attacks lasting for several hours. We cannot tell much about the prognosis.

CASE 2.—*Novasurol in Cardiac Edema in Childhood.*—In connection with this case, I wish to bring up the question of the treatment of edema in some patients with badly decompensated hearts. I have used novasurol in five children in this condition. The first child was very edematous and nothing else had helped at all. The urinary output in the first four days was between 50 and 200 cc. each day. On the fifth day, I gave an ampule of novasurol, and the output increased slightly. Four days later, I gave another ampule and the output increased to 3,400 cc., but there were no permanent results. The child died several days later, and at necropsy we found present a condition similar in type to that reported before following the use of novasurol. There were several ulcerative areas in the transverse colon, which our pathologist stated were definitely due to a chemical cause. I do not think this had anything to do with the child's death. One injection was given in the leg, which, at the time, was very edematous, and a large area of induration resulted. The second case we used it in was that of a boy, aged 10 years, whose urinary output varied between 50 and 600 cc. daily. We first gave half an ampule and obtained no results. Four days later we gave a full ampule and the output increased moderately, but the child died within twenty-four hours. The next patient was very edematous, with a large amount of ascites. We gave half an ampule and obtained an output of 1,000 cc. Three days later we gave another ampule with no result. Four days later we gave a third ampule, and obtained an output of 400 cc. After the last ampule we gave before he died, there was an output of 3,685 cc.

The patient here presented is the only one who survived the decompensation. She came into the ward in May suffering from edema and weighing 52 pounds; in four days she weighed 56 pounds. On the seventh day we gave her half an ampule of novasurol, and the urinary output increased and continued markedly increased for four or five days. We gave another half an ampule and the output increased to 1,400 cc. The last ampule we gave brought an increase to 1,600 cc. Since then, the edema has gradually subsided and her condition has greatly improved. She has been up for a month or six weeks.

We do obtain results from the use of novasurol, for there is usually a marked increase in the output of urine following its use, but this improvement is not lasting in cases of bad decompensation. I think this is due to the fact that we are dealing with an infectious process, and even though we are able to eliminate a vast amount of the fluid by means of the novasurol, we are not able to keep far enough ahead of the condition in the heart for it to recover sufficiently so that the increased output is continued.

CYSTIC LYMPHANGIOMA. Presented by DR. JOHN L. REICHERT.

Three cases were presented. In the first two the tumor was located in the neck. These two cases showed the following characteristics in common: The tumors were present at birth, fluctuated, were compressible, but not reducible, very easily transilluminable and were multilocular. The skin was freely movable over them, and the tumors were freely movable on the underlying tissues. In the first case the tumor was superficial, flabby and grew only with the growth of the child. It was not susceptible to direct hematogenous or lymphogenous infection. The contents were orange colored and sterile. In the second case the tumor was deeper, more tense and was very susceptible to direct and lymphogenous

infection, although for the first six months of life it was quiescent. It eventually grew widely and extended deeply in spite of roentgenotherapy and radium. At necropsy, it was found that the tumor had extended into the chest cavity, and the axilla and had eroded the trachea. The contents were purulent and contained staphylococci and streptococci.

These two cases were shown as two distinct types of cystic lymph vascular tumors. It was suggested that the innocent types as illustrated by the first case be called cystic lymphangiectasis and that the term cystic hygroma be reserved for the neoplastic type as illustrated by the second case. A more descriptive term for this type is lymphangio-endothelioma.

The third case was a so-called sacral hygroma. Clinically, it resembled the neoplastic type of cervical tumor. The nature of sacral hygromas is not clear. They are extremely rare, and may be lymph vascular in origin.

A differential diagnosis of the cervical and sacral tumors was given, and the various methods of treatment were discussed.

JUVENILE TABES DORSALIS. Presented by DR. HAROLD A. ROSENBAUM.

CASE 1.—This patient, a girl, came to the hospital in January, 1925, with a history of acute abdominal pain of two days duration, associated with vomiting. The early history is negative for rash, snuffles or disturbance of nutrition of the nails. She walked at 9 months and talked well at 1 year. When she was admitted to the hospital she was a pale, rather undernourished and undersized child, aged 7½ years. The epitrochlear nodes were the size of small peas. The pupils did not react to light or in accommodation, the right was a trifle smaller than the left and both were dilated. The tendon reflexes were normal and there was no incoordination. A Wassermann blood test was made, which was ++++, as was the spinal fluid. The globulin reactions were positive, the Lange reaction was 544432111. In February, the patient fell down stairs and fractured her right ulna and displaced her right radius. This caused no pain and the reduction was done without an anesthetic and was almost painless. The first reduction was unsatisfactory and it was reduced a second time, still without pain. In August she came to the dispensary with a well developed herpes zoster over the left buttock, extending over the left side of the vulva. About ten days later the mother asked me to come to see the child. She had had another attack of acute abdominal pain accompanied by vomiting. I saw her at about the end of the attack, which had lasted for four days. She lay with her eyes closed and did not notice anything. The abdomen was soft, there was no tenderness, the pharynx was negative and there was no fever. The child later described the pain, "Like someone was cutting me." Because of the character of the pain, the nonreacting pupils and painless fracture, and the herpes which sometimes accompanies tabes dorsalis, we thought that the child had passed through an attack of abdominal crisis of tabes dorsalis. As Dr. Cheney said, juvenile tabes is much more rare than juvenile paresis and the clinical picture is usually incomplete. In this girl the deep reflexes are still present, although the Achilles jerks are less active than they have been. The course is very slowly progressive. At the end of the second decade the patient is incapacitated.

CASE 2.—*Vitiligo.*—This patient is a colored boy who came to the hospital in 1922 because of interstitial keratitis. The Wassermann reaction was positive and he was placed on suitable treatment. I did not see him until the next December. In the meantime he had been at the Cook County Hospital where he had received treatment. The interstitial keratitis had increased, and he developed corneal ulcers which perforated with resulting complete loss of vision. The condition for

which we are showing him today, however, is this complete patchy loss of pigments or vitiligo which you see. Previous to the development of this skin condition there was a blotchy rash which lasted a few days, without fever or subjective symptoms. A rash often precedes pigment atrophy. This vitiligo began on the side of the head, and then appeared on the dorsal surfaces of the extremities and in some places on the body. It progressed for about six months and then became stationary. The same picture has been present since November, 1922. This condition is not uncommon on a basis of syphilis, although it may be found in other infections such as leprosy, in some skin diseases such as lichen planus, and is met in some of the general states such as in myxedema, nervous exhaustion and at the time of the menopause.

PURPURA HEMORRHAGICA COMPLICATED BY A FLACCID HEMIPLEGIA. Presented by DR. MARGARET W. GERARD.

This child has had purpura hemorrhagica for eight months. She was admitted to the hospital four months after the onset of the disease in a severely toxic condition, with convulsions of the left side. At no time during the two months' course of the hemiplegia did she develop a spastic stage. There was a gradual return of reflex activity and motor power, so that, at the present time, there is no evidence of any difference between the two sides. This type of paralysis, of course, is very rare following hemorrhage into the brain. Lewandowsky and Dejerine both mention its rare occurrence, and Dr. Thor Rothstein has found such paralyses following hemorrhage anterior to the motor area, and in certain other extrapyramidal lesions.

Although the patient has entirely recovered from the paralysis, the purpura is still present. There have been exacerbations alternating with periods of improvement, but at no time has the blood picture entirely returned to normal.

CHLOROMA. Presented by DR. G. L. KAUFMANN.

CASE 1.—This child entered the hospital with a history of bulging of the eyes. Two weeks previously there was marked lassitude, the child felt ill and did not play. Six months before this attack the eyes had been examined because of frontal headache and glasses were prescribed. On admission to the hospital there was bulging of both eyes, more marked on the right, and the right pupil was larger than the left. There was tenderness and pressure in both ears, but the drums were negative. The glands were swollen, the ethmoid was negative. The Wassermann reaction was negative, the Pirquet positive. The bulging of the eyes persisted and two days later the patient developed paralysis of the right side of the face. One roentgen-ray treatment caused slight improvement, but two days after the treatment she began to get worse. We believe it is a case of chloroma, which has been regarded as a malignant form of leukemia. (Necropsy later revealed the green tumor.)

CASE 2.—*Scurvy.*—This girl, aged 18 months, came in with tenderness and swelling of the leg, and a history of having fallen out of a baby carriage. The question of traumatism was considered, but roentgen-ray examination and the finding of a bluish discoloration around the gum caused a diagnosis of scurvy to be made. She had marked calcification of the lower end of each femur.

MULTIPLE LUNG ABSCESS FOLLOWING TONSILLECTOMY? Presented by DR. JOSEPH BRENNEMANN.

CASE 1.—This child had a tonsillectomy performed at a west side hospital. Two or three days later she developed a high temperature, and was admitted to

this hospital on Sept. 12, 1925, very ill. She was examined carefully, but nothing was found except a little dulness in the axillary line, but roentgen-ray examination showed three shadows that we thought were multiple lung abscesses. After eleven days, during which the temperature remained very high, the areas had increased in size, and we decided to call in a bronchoscopist. The morning after the bronchoscopy and bronchotherapy, the expectoration had a foul odor and this was present during the bronchoscopy. The child then developed a pneumothorax, and was very ill. The following morning she was better, and has made an uneventful recovery in about ten days. She is now perfectly well and gained 8 pounds in four weeks.

In the ordinary sense of the word, this could not have been a real lung abscess. In another case a small rubber stopper slipped into a bronchus and the child had a massive collapse of the lung. The lung cleared up entirely a few days after the plug was removed by Dr. McGinnis. It is my opinion that something from the throat became plugged in the bronchus in the present case, and in the bronchoscopic treatment the plug was removed.

Case 2.—*Keratodermia Plantaris et Palmaris.*—This child has been our most interesting patient for about a year. He has been shown before the Chicago Dermatological Society and the Pediatric Society; photographs have been sent to other centers in an effort to get a correct diagnosis. He is now about 6 years old. The lesions of the palms and soles have remained about the same while under our observation. Around the mouth there are areas of hyperkeratosis, and these are also present on the feet, hands, arms and umbilicus. One finger and one thumb have lost the distal joint. The feet show the thick skin lesions. There are some lesions about the umbilicus and there is a crater-like lesion in the rectum that goes in some distance.

As to diagnosis, some of the dermatologists suggested acrodynia. Syringomyelia has been suggested and also a gonococcus infection of the skin. I believe it is a case of what has been called *keratodermia plantaris et palmaris.* No cases have been reported with lesions around the face and the anus. An interesting feature is that Dr. Peterman of the Mayo Clinic said that they had a case just like this one, including the lesion about the rectum. The question of leprosy comes up, but I do not think any of the signs present here are ever present in leprosy. The case will be reported in detail later by Dr. H. C. Olmstead, of Seattle.

The Diagnostic Value of Quantitative Determination of Cerebrospinal Fluid Sugar in Encephalitis and in Meningitis. Presented by Dr. E. R. Carlo.

This is a preliminary report on the sugar content of the cerebrospinal fluid in nineteen cases of encephalitis, thirty-one cases of tuberculous meningitis, and one case each of influenzal and streptococcus meningitis. The diagnosis in each case was based on the clinical signs and symptoms, and on the laboratory findings.

Attention is called primarily to the findings in the encephalitis cases, the findings in the meningitis cases being included for comparative purposes. The Folin-Wu method was used for the determination of the sugar.

Because of these findings, we believe that the quantitative determination of the cerebrospinal fluid sugar is of value not only in making a diagnosis of encephalitis, but also in differentiating that condition from tuberculous meningitis and the purulent types of meningeal involvement, when the clinical picture is confusing.

TABLE 1.—*Cerebrospinal Fluid Sugar (Mg. Per 100 cc. Spinal Fluid)*

Encephalitis 19 cases 28 determinations	Tuberculous Meningitis 31 cases 33 determinations	Meningococcus Meningitis 7 cases 7 determinations
1. 152	1. 80	1. 65
2. 132	2. 54	2. 26
3. 105	3. 48	3. 26
4. 98	4. 45	4. 24
5. 95	5. 45	5. 21.4
6. 95	6. 45	6. 18.2
7. 94	7. 44	7. 10
8. 92	8. 40	
9. 92	9. 38	
10. 90	10. 38	
11. 90	11. 36	
12. 89	12. 36	Influenzal Meningitis
13. 87	13. 36	1. 26
14. 87	14. 35	
15. 85	15. 35	
16. 82	16. 34	
17. 80	17. 34	
18. 78	18. 30	Streptococcus Meningitis
19. 78	19. 30	1. 22.5
20. 76	20. 30	
21. 70	21. 30	
22. 70	22. 28	
23. 70	23. 27	
24. 66	24. 27	Averages
25. 66	25. 26	Encephalitis. 85.3 mg.
26. 64	26. 26	Tuberculous meningitis. 33.7 mg.
27. 60	27. 26	Purulent types. 25.6 mg.
28. 56	28. 24	
	29. 20.4	
	30. 20	
	31. 19.4	
	32. 18	
	33. 10	

TABLE 2.—*Comparison of Height of Thoracic and Abdominal Curves*

Diagnosis	Total Number Cases	Thoracic Movement Greater				Abdominal Movement Greater			
		Number Cases	Per Cent Greater			Number Cases	Per Cent Greater		
			Lowest	Highest	Average		Lowest	Highest	Average
Normal	10	1	..	...	66	9	8	180	58
Acute appendicitis	6*	5	19	280	110	0	..	...	..
Appendicitis ruptured or with abscess	8	7	57	300	136	1†	..	...	4
Subacute appendicitis	2	0	..	...	..	2	34	100	67
Chronic appendicitis	1	0	..	...	..	1	..	...	100
Lobar pneumonia with abdominal pain	6*	1	..	...	19	4	45	100	83

* In one case curves equal in height.
† No abdominal tenderness.
All cases of appendicitis were operated on.

CLINICAL RESULTS WITH VARIOUS FORMS OF TREATMENT IN NEPHROSIS. Presented by DR. C. A. ALDRICH.

Charts illustrating the body weight and urinary output curves in eighteen attacks of generalized edema occurring in eight patients with nephrosis were shown. The method of treatment, including dietary regimens, administration of alkalis, diuretics, cathartics, the application of various dehydrating measures and the surgical treatment of accompanying infections of the upper respiratory tract were indicated in each instance.

The results were summarized as follows:

1. Administration of alkalis, diuretics, cathartics, dehydrating measures and of the various dietary regimens exerted no constant beneficial result on the course of the disease.

2. Whenever it was possible to afford immediate relief from intoxication of infectious origin, reduction of edema suddenly followed.

SIMULTANEOUS KYMOGRAPHIC TRACINGS OF THORACIC AND ABDOMINAL RESPIRATORY MOVEMENT IN APPENDICITIS AND IN PNEUMONIA WITH ABDOMINAL SYMPTOMS.* Presented by DR. W. B. MCCLURE.

The object of this study is to determine whether or not a comparison of the abdominal and thoracic respiratory movements, as simultaneously recorded in kymographic tracings, may be of aid in differentiating lobar pneumonia with abdominal symptoms simulating appendicitis from acute appendicitis.

It is well known that immobility of the abdominal wall is found in typical cases of acute appendicitis with peritoneal involvement, and that abdominal pain and tenderness, with at times a defensive muscular rigidity, may occur in lobar pneumonia.

Apparatus.—The apparatus used consists of two tubular pneumographs of the type described by G. W. Fitz in 1896, modified somewhat so as to be more suitable for use with children. These pneumographs are connected by rubber tubing to Marey tambours which operate writing levers. One pneumograph is placed around the abdomen at the umbilicus. Similar increases in girth of the chest and of the abdomen produce curves of approximately equal height. The ages of the children studied ranged from 2 to 2½ years.

It should be noted that, whereas the thoracic curves were higher than the abdominal curves in all but two of the cases of acute appendicitis, ruptured appendix, and appendiceal abscess, the reverse was in general true for the cases of lobar pneumonia with abdominal symptoms in which the abdominal movement was greater in four, less in one, and equal in one.

In acute appendicitis and lobar pneumonia with abdominal pain in children, it would seem that the determining factor in the location of restriction of respiratory movement is the site of the lesion causing pain. With the lesion in the abdominal cavity (peritonitis) the abdominal movement is restricted, and with the lesion in the pleural cavity (pleurisy) the thoracic movement is restricted, if there is any restriction.

While a larger series of cases is necessary for definite conclusions, it is suggested that a graphic method of comparing thoracic and abdominal movement might prove to be an aid in differentiating the pseudoappendicitis of lobar pneumonia from acute appendicitis.

---

* Dr. C. J. Eldridge collaborated in the early part of this study, during the period of adaptation of the apparatus and of the recording of the first cases of appendicitis.

SENSITIZATION. Presented by DR. FRANKLIN J. CORPER.

Four patients were presented, one was sensitive to fish, one to egg and barley, one to wheat and one to orris root. In the first case there was a typical food idiosyncrasy, which was similar to the anaphylaxis found in the lower animals. The second case was the type that makes one enthusiastic in extolling the virtues of protein sensitization as applied to eczema. In the third case there was a paradoxical situation, in that the child improved clinically when wheat was added to the diet, but gave a positive reaction to wheat. In the fourth case, the child had asthma, and with the skin reaction to orris root one might expect that it played some part in the disease, but such was not the case. The cases were presented as a warning to those who may have happy terminations in a few fortunate cases to therapy based on specific reactions applied to the skin or intracutaneously. Before making a diagnosis of protein sensitization, certain factors should be taken into consideration: 1. The test with proteins. 2. The distinct improvement of manifestations within a few days after withdrawal of the offending protein. 3. The distinct increase in the symptoms of any subacute case.

Book Reviews

INDIVIDUAL GYMNASTICS. Revised. Third edition. Edited by LILLIAN CURTISS DREW. Pp. 275, with 121 engravings. Price, $2.25. Philadelphia: Lea and Febiger, 1926.

This is a handbook of corrective and remedial gymnastics, based on the author's experience in individual gymnastics. It presents to those interested in physical education the causes and treatment of certain physical defects, with especial reference to the individual who requires special training other than the regular gymnastic lesson.

The author emphasizes the prophylactic, as well as the therapeutic phase, and at the same time advocates the cooperation of the gymnastic instructor with the orthopedic surgeon.

This book will be of the most value to physical directors, who have large groups and especially to those who employ gymnastic exercises according to the individual case.

Its content is divided into 16 chapters, which deal with gymnastics, the fundamental anatomy of the framework of the human body, various postures and the correction of faulty postures.

The chapters on shoes and the feet are important features of the text, and although there is some variation of opinion on these subjects, it is all that could be expected in such a text. Another on infantile paralysis, since it causes so many conditions which require special training, constitutes an important chapter.

The book is very well edited and the publishers have printed it on good paper with clear type. Some of the illustrations are from photographs, but many are sketches showing various positions of the individual in the exercises.

THE CLINICAL STUDY AND TREATMENT OF SICK CHILDREN. Edited by JOHN THOMSON, M.D., LL.D., F.R.C.P. Fourth revised and enlarged edition. Price, 30 shillings. Pp. 912, illustrated. Edinburgh and London: Oliver and Boyd, 1925.

In many present day treatises, the clinical side of medicine is so lost in a maze of scientific speculation that it is a relief to take up this book by the dean of Scottish pediatricians. The wealth of clinical experience and the keenness of perception which these pages reveal is rarely encountered. Laboratory diagnostic methods are not ignored, but are given their rightful place as adjuvants to examination of the patient. The patient is always before the reader, not the disease. If one expects an exhaustive discussion of the whole field of pediatrics, the book will not satisfy. For instance, contagious diseases are only rather casually mentioned. But if his desire be to have a word picture of the disease manifestations in the sick child, he will look far before he finds one that is better. The illustrations are numerous and well chosen to depict the conditions which they elucidate. On the whole, an excellent book by a trained clinical observer of the old school.

LA TERRAIN HEREDO-SYPHILITIQUE. By V. HUTINEL. Pp. 455. Price, 30 francs. Illustrated. Paris: Masson et Cie., 1926.

This volume is an exhaustive treatise on the subject of congenital syphilis, not only from the standpoint of the actual pathology but also from the standpoint of

the possible relation of syphilis to various other diseases. One who is familiar with the French literature soon gains the impression that most French writers attribute to syphilis a much wider complicity as an etiologic factor in various diseases than do American writers. This impression is strengthened when perusing this book. It is noticeable that the references in the text are nearly all to French publications. Almost no reference is made to recent American work along this line. On the whole, the book is good, and contains much that is valuable.

ANTHROPOLOGY OF EASTERN CHINA AND KWANTUNG PROVINCE. By S. M. SHIROKOGOROFF. Pp. 162. Price, $2.50 (Chinese). Shanghai, China: Commercial Press, 1925.

PROCESS OF PHYSICAL GROWTH AMONG THE CHINESE. Vol. 1. The Chinese of Chekiang and Kiangsu. By S. M. SHIROKOGOROFF. Pp. 167. Price, $6.00 (Chinese). Shanghai, China: Commercial Press, 1925.

These two interesting volumes contain many careful measurements, together with deductions of an anthropological nature on Chinese. To one interested in the subject they should prove valuable.

THE AMERICAN JOURNAL OF DISEASES OF CHILDREN is published by the American Medical Association as a means for the advancement of knowledge of the diseases of children and for the publication of scientific investigation in this field.

Manuscripts for publication, books for review, and correspondence relating to the editorial management should be sent to Dr. Clifford G. Grulee, 104 South Michigan Avenue, Chicago, or to any other member of the Editorial Board. Communications regarding subscriptions, reprints, etc., should be addressed, AMERICAN JOURNAL OF DISEASES OF CHILDREN, American Medical Association, 535 North Dearborn Street, Chicago.

Articles are accepted for publication on condition that they are contributed solely to the AMERICAN JOURNAL OF DISEASES OF CHILDREN. Manuscripts must be typewritten, preferably double spaced, and the original copy should be submitted. Zinc etchings and halftones of illustrations will be supplied by the Association when the original illustrations warrant.

Footnotes and bibliographies should conform to the style of the Quarterly Cumulative Index, published by the American Medical Association. This requires, in order given: name of author, title of article, name of periodical, with volume, page, month—day of month if weekly—and year. A complete list of abbreviations for standard periodicals, together with a full discussion of the style of the A. M. A. publications, appears in The Art and Practice of Medical Writing, a comprehensive book on the preparation of medical manuscripts, published by the American Medical Association. Price, $1.50.

Matter appearing in the AMERICAN JOURNAL OF DISEASES OF CHILDREN is covered by copyright; but, as a rule, no objection will be made to its reproduction in reputable medical journals, if proper credit is given. However, the reproduction for commercial purposes of articles appearing in the AMERICAN JOURNAL OF DISEASES OF CHILDREN or in any one of the other publications issued by the American Medical Association will not be permitted.

Authors will receive one hundred reprints free; additional reprints may be obtained at cost.

The AMERICAN JOURNAL OF DISEASES OF CHILDREN is published monthly. Annual subscription price (two volumes): Domestic, $4.00; Canadian, $4.30; foreign, $4.50, including postage. Single copies, 50 cents, postpaid.

Checks, etc., should be made payable to the AMERICAN MEDICAL ASSOCIATION.

OTHER PERIODICAL PUBLICATIONS
of the American Medical Association

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION—Weekly. Covers all the medical sciences and matters of general medical interest. Illustrated. Annual subscription price (two volumes): Domestic, $5.00; Canadian, $6.50; foreign, $7.50. Single copies, 20 cents.

ARCHIVES OF INTERNAL MEDICINE—Monthly. Devoted to the publication of advanced, original clinical and laboratory investigations in internal medicine. Illustrated. Annual subscription price (two volumes): Domestic, $5.00; Canadian, $5.40; foreign, $5.75. Single copies, 75 cents.

ARCHIVES OF NEUROLOGY AND PSYCHIATRY—Monthly. A medium for the presentation of original articles on nervous and mental diseases, with abstracts from foreign and domestic literature, book reviews, society transactions, etc. Illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75. Single copies, 85 cents.

ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY—Monthly. Devoted to advancing the knowledge of and progress in cutaneous diseases and syphilis. Publishes original contributions and full abstracts of the literature on these two subjects, transactions of the important dermatological societies, book reviews, etc. Illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75. Single copies, 85 cents.

ARCHIVES OF SURGERY—Monthly. Devoted largely to the investigative and clinical phases of surgery, with monthly reviews on orthopedic and urologic surgery. Well illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75. Single copies, 85 cents.

ARCHIVES OF OTOLARYNGOLOGY—Monthly. A medium for the presentation of original articles on diseases of the ear, nose and throat, with abstracts from foreign and domestic literature, book reviews, the transactions of special societies, etc. Illustrated. Annual subscription price (two volumes): Domestic, $6.00; Canadian, $6.40; foreign, $6.75. Single copies, 75 cents.

ARCHIVES OF PATHOLOGY AND LABORATORY MEDICINE—Monthly. A periodical devoted to the publication of original contributions in the field of pathology, with abstracts from foreign and domestic literature, book reviews, the transactions of special societies, etc. Illustrated. Annual subscription price (two volumes): Domestic, $6.00; Canadian, $6.40; foreign, $6.75. Single copies, 75 cents.

QUARTERLY CUMULATIVE INDEX TO CURRENT MEDICAL LITERATURE—Quarterly. A complete subject and author index to the worth-while current medical literature of the world. Issued four times a year. Second and fourth volumes bound for permanent reference. Subscription price, calendar year: Domestic, $8.00; Canadian, $8.50; foreign, $8.75.

AMERICAN MEDICAL ASSOCIATION

535 North Dearborn St. CHICAGO

American Journal of Diseases of Children

VOLUME 31 MAY, 1926 NUMBER 5

THE PREVENTION OF RICKETS

THE INFLUENCE OF THE ROUTINE ADMINISTRATION OF COD LIVER OIL IN THE PREVENTION OF RICKETS IN INFANTS*

MAY G. WILSON, M.D.

NEW YORK

It is a common experience in outpatient and private practice to observe rickets develop in infants who are receiving cod liver oil. The potency and dosage of the cod liver oil given is, as a rule, questioned. However, we do see infants with rickets who have received, over a prolonged period, the usual amounts of a well recommended cod liver oil.

In view of the universal routine administration of cod liver oil for the prevention of rickets, it seemed timely to investigate the subject. Such an investigation was undertaken in the outpatient department of the New York Nursery and Child's Hospital. It extended over a period of two years (1923-1925), and included observations on 210 infants. Of this number, 132 received cod liver oil. The remaining seventy-eight who did not receive cod liver oil were included as control cases.

At first, it seemed best to determine the approximate incidence of rickets in infants attending the outpatient clinic. A survey was made in March, 1924, and the case records of sixty-three infants, aged from 3 to 10 months, were arbitrarily selected for study. The only special selection of cases was that limited to age and regularity of attendance. The group included forty-nine babies, to whom cod liver oil was prescribed in a daily dosage of one-half to one and one-half teaspoonfuls. The administration of cod liver oil (which was obtained from the drug department of the hospital),[1] was begun between the ages of 1 and 3 months. Fourteen babies who had not received cod liver oil were included as controls. No special supervision had been instituted to insure the administration of the cod liver oil, and these infants received the routine social service supervision of the clinic. The cooperation of the mother was indicated by a record of regular attendance.

The information obtained from the charts necessarily included examinations by several of the attending staff. The criteria of diagnosis were clinical, being based on the usually accepted signs of rickets as recorded in the case histories. The data obtained disclosed demonstrable rickets in

* Received for publication, Dec. 18, 1925.

* From the Department of Pediatrics, Cornell University Medical College, and the Pediatric Service of the New York Nursery and Child's Hospital.

1. This oil was purchased from a reputable firm in five gallon containers, and was sold as pure Norwegian oil.

CONTENTS

PAGE

Biliary Cirrhosis: Report of a Case with Atresia of the Intrahepatic but without Atresia of the Extrahepatic Bile Ducts, and with a Study of its Metabolism. Leonard G. Parsons, M.D., F.R.C.P. (London), and Evelyn M. Hickmans, Ph.D., M.Sc. (Birmingham), Birmingham, England 459

Chronic Interstitial Hepatitis, with Report of a Case. George F. Munns, M.D., Chicago 469

Death Following the Inhalation of Zinc Stearate. Karl Schlarpfer, M.D., Milwaukee 474

Defects in the Membranous Bones, Diabetes Insipidus and Exophthalmos: Report of a Case. Bernard S. Denzer, M.D., New York 480

Syphilitic Endarteritis in Children. Harry M. Gilkey, M.D., and C. C. Dennie, M.D., Kansas City, Mo. 483

Erythema Infectiosum: A Clinical Report of Seventy-Four Cases. Theodore P. Herrick, M.D., Cleveland Heights, Ohio 486

The Respiratory Metabolism in Infancy and in Childhood: III. Glycogen Storage in Children. Samuel Z. Levine, M.D.; James R. Wilson, M.D., and Helen Rivkin, M.A., New York 496

Uric Acid and Creatinin in the Urine of Infants. O. S. Rougichitch, M.D., Boston 504

Plasma Chlorides in Acute Intestinal Intoxication of Children. Gladys L. Boyd, B.S., M.D. (Tor.), Toronto, Canada 514

A Quantitative Method for the Determination of the Combined Urea and Ammonia Nitrogen of Saliva. Frederic W. Schlutz, M.D., and Mildred R. Ziegler, M.S., Minneapolis 520

Paratyphoid Fever: Report of a Case in an Infant. David Gingold, M.D., and Harry Wexler, M.D., Brooklyn, N. Y. 522

Progress in Pediatrics:

Appendicitis in Children under Five Years of Age. Frederick Christopher, M.D., Winnetka, Ill. 525

Correspondence:

Contribution to the Rickets-Tetany Problem. Charles Waltner, M.D., Baltimore 548

News and Comment 549

Abstracts from Current Literature 551

Society Transactions:

Central States Pediatric Society 590

Book Reviews 601

A further analysis of the age period at which the evidence of rickets was first observed both clinically and by roentgen ray is shown in table 2. It is of importance to note that at 3 months of age 27 per cent showed clinical evidence, and 44 per cent roentgenographic evidence of rickets. By the fourth month, clinical rickets was observed in 38 per cent and roentgenographic evidence of rickets in 82 per cent. The development of rickets in these infants, despite the administration of a potent cod liver oil in the usual amounts, requires some explanation. The following factors may be considered: 1. Was the usual dosage of cod liver oil prescribed too small? 2. Should cod liver oil be administered before the age of 3 months to prevent the development of rickets?

WINTER SERIES

With these considerations in mind, a final study was undertaken on eighty-seven infants, aged from 1 to 3 weeks. These infants were born in the winter of 1924 and 1925 in the in-door and out-door obstetric service of the hospital. The entire group was organized as a special class for the prevention of rickets in infants. All of the subjects were healthy infants born at term, the majority being breast fed. The various races were equally represented. Some of the infants resided in the suburbs of the city, the majority comprising the better class of patients attending the clinic. This class was in charge of a social worker of unusual personality, who made the home contact and insured an unusual *esprit de corps* among the mothers. The initial examination and succeeding ones were made by one medical examiner. The clinic was held weekly, appointments being made at least every three weeks. During the months of February and March, infants were seen bimonthly.

Fifty-three infants of this group were prescribed cod liver oil from the age of 2 weeks, in the following dosage: one-half teaspoonful daily at 2 weeks of age; one teaspoonful daily at 1 month of age; two teaspoonfuls daily at 2 months of age; three teaspoonfuls daily at 3 months of age; from three to four teaspoonfuls daily for the remaining period of observation. The administration of the cod liver oil was given special attention. The amount prescribed, purchased and given was checked at clinic and home visits. Factors such as refusal, vomiting or any irregularity of administration of cod liver oil were recorded at each visit. In the final analysis of the total amount of cod liver oil actually taken by each infant, all these factors were taken into consideration. The cases were grouped according to the amount of cod liver oil taken. It was found that 51 per cent received and retained the maximum amount prescribed; 31 per cent of the infants were given the maximum amount but were observed to regurgitate at times, and 14 per cent of the infants received and retained the maximum amounts, except for occasional lapses of less than one week's duration. In six, the investigation was dropped because

55 per cent of the infants receiving cod liver oil. This may be considered a conservative index of the incidence of clinical rickets in this clinic, in which cod liver oil is prescribed routinely for the prevention of rickets. It should be noted here that the cod liver oil may not have had the required antirachitic potency, or that the oil may not have been given regularly. The control group of fourteen cases showed rickets in 28 per cent; however, the latter infants were chiefly under 6 months of age, when the clinical diagnosis is not easily made.

SUMMER SERIES

In the succeeding investigation, an effort was made to insure the routine administration of a potent cod liver oil. This study included sixty infants born in the spring and summer of 1924, when they were from 1 to 3 months of age; all of these were registered in the outpatient clinic. Although these infants remained under the general care of the clinic physician, they were referred monthly for examination. At these times, roentgenograms of the distal ends of the ulna and radius were taken, and examination of the infant was recorded at each visit by the same medical examiner. A special social worker was in charge of these babies, and every effort was made to secure the intelligent cooperation of the mother. The importance of truthfulness in reporting accurately concerning the administration of the cod liver oil was stressed. The cod liver oil [2] dispensed was biologically tested and certified by a reputable firm; the amount prescribed was sufficient to last until the next clinic visit, and the daily dosage was increased from one-half teaspoon to one and one-half at three months, the latter dose being the maximum, which was continued until the infant was 1 year of age. Nineteen of these infants who had not received cod liver oil were used as controls, and were referred only for initial and confirmatory clinical and roentgenographic examinations.

RESULTS

At the completion of these observations in the fall, the subjects were between the ages of 6 months to 1 year. A summary of these results are presented in detail in table 1. Here it may be seen that for infants receiving cod liver oil, 2 per cent did not reveal any clinical evidence of rickets, 4 per cent showed only a single manifestation, and 91 per cent developed two or more rachitic signs. For infants not receiving cod liver oil, 21 per cent showed only a single rachitic manifestation and 76 per cent two or more. (These infants were only seen on initial and final examinations. The data were obtained from the clinic charts.) Confirmatory roentgen-ray evidence of rickets was obtained in practically 100 per cent for both groups. It is evident, then, that the majority of these infants developed rickets, there being little real difference between infants receiving and those not receiving cod liver oil.

2. An American oil obtained from the Newfoundland coast.

respiratory infection. The final diagnosis of rickets was based on the presence of more than one of the manifestations usually considered rachitic. At the completion of the observations, each case record was analyzed and graded as follows: Normal (no rachitic manifestation); queried or plus minus, questionable (having indefinite or but one major rachitic manifestation recorded); 1 plus, mild rickets (having more than one definite rachitic manifestation); 2 and 3 plus, moderate rickets (having two or more definite rachitic manifestations); 4 plus, severe rickets (having marked and numerous rachitic manifestations). The summary of these findings is shown in table 1.

ROENTGENOGRAPHIC DIAGNOSIS OF RICKETS

Roentgenograms were taken of the wrists, the position of the hands being with palms upward. As far as possible, the same technic [4] was maintained during the entire period of investigation; films were read weekly and the series was reread at the completion of the study. As a rule, doubtful readings were confirmed by succeeding films. Owing to the character of the early rachitic changes, as well as to the position of the wrists, roentgenographic diagnosis is frequently impossible from one roentgenogram.

In roentgenogram readings, the distal ends of the shafts of the ulna and radius were particularly studied. Normally, the contour of the metaphyseal margins of the ulna and radius is convex and sharply defined; the structure of the shaft is fine and appears homogenous. The earliest roentgenographic rachitic changes observed were hair-like threads or projections from the distal end of the shaft of the ulna, less frequently the radius, progressing in succeeding films to definite fraying and fringing, the contour of the end of the shaft of the ulna becoming ill defined and widened with sharp corners. The later changes observed were the familiar ones of cupping, with coarsening of the structure of the shaft of the bone. With healing, the evidence of rickets became more intensified, irregular bands and shadows due to lime salt deposits appeared at the distal ends of the ulna in the zone of preparatory calcification and along the shaft. In final roentgenograms, the contour of the bone appeared normal, although evidence of previous rickets still

4. The roentgenograms were taken by Misses Devereaux and Clauson in the roentgen-ray department of the hospital under the direction of Dr. I. Liss; the technic being:

Baby, thin: milliamperage, 30; backup, 3½; kilovolts, 70; rheostat, 9; time, one-third to one-half second.

Baby, medium: milliamperage, 30; backup, 3½; kilowats, 70; rheostat, 10; time, one-third to one-half second.

Baby, fat: milliamperage, 30; backup, 3½; kilovolts, 70; rheostat, 11; time, one-half to three-fourths second. Every plate was taken at 20 inch distance, small cone, fine focus, Coolidge tube. The plates developed very black.

of irregularity of cod liver oil therapy. In a study of this character, it would seem that the administration of the cod liver oil was insured as far as possible.

A record was also kept of the average number of hours of open air and sunlight given each infant daily. The cod liver oil dispensed was biologically assayed once during the course of the year by the producers, to determine the presence and concentration of the antirachitic factor; this was reported to be up to the standard required.[3]

The control group of this series, numbering thirty-four infants, were given the same medical and social service supervision, with the exception of the cod liver oil therapy. In addition, twelve were instructed as to exercise and massage, which consisted of daily passive and active movements and massage of extremities, using cocoa butter, one to three times daily. The remaining eighteen (four were dropped), were instructed as to daily sun baths and were prescribed one-half teaspoon of an inert mineral oil to insure their interest. The amount and regularity of massage was graded and given as follows: six infants, massage and exercise three times a day; four received massage and exercise once a day; in two, massage and exercise were given irregularly. The amount of direct sunlight given was recorded; seventeen infants did not receive any direct sunlight; eleven were occasionally exposed on warm days; two were out in arms or in uncovered carriages from one to three hours in good weather.

CRITERIA OF DIAGNOSIS

Before analyzing the results of the observations of this study, it would seem best to define the criteria of diagnosis used.

The examinations were recorded on special charts, which included notations as to general condition, weight, shape of head, size of fontanel, presence of cranial bosses and craniotabes. The latter finding was limited to definite softness of the parietal and occipital bones, developing under observation. This was differentiated from the yielding of the bones of the cranium in new-born infants, particularly near fontanels and sutures. The costochondral junctions of the fifth and seventh ribs were particularly examined. The grade of beading was noted, namely, minus, as found at birth; 1 plus, slightly prominent; 2 plus, moderately enlarged; 3 plus, greatly enlarged. The 2 and 3 plus gradings were considered as rachitic rosaries. The enlargement of the epiphyses and the presence and degree of flaring ribs and bowing of the legs were graded similarly. Special note was made of muscular development, dentition, constipation, restlessness, perspiration of the head and repeated

3. Report from the scientific department of Mead, Johnson and Co., shown from samples submitted, using the line test technic, a 2 + healing in rats kept in a totally dark room, which is the standard required.

TABLE 1.—*Comparative Incidence of Clinical, and Roentgen-Ray Evidence of Rickets, Among Infants Receiving and Not Receiving Cod Liver Oil* *

	Age of Examination, Months	Per Cent Normal or Doubtful	Per Cent Rickets at	Clinical Diagnosis			Rickets				Per Cent Normal	Per Cent Rickets	Roentgen-Ray Diagnosis					
				No. Cases Normal	Doubtful ?	Doubtful +—	Mild +	Moderate 2+	Moderate 3+	Severe 4+			Normal	ED	AD	A	B	C	D
36 Cases—Summer Series Receiving Small Doses of Cod Liver Oil from 1 to 3 months to 1 year of age	2-3	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
	3-4	2.7	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..
	4-5	..	2	..	..	..	..	..	..	1	..	5	..	..	..	1	1	..	..
	5-6	2.7	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
	6-7	..	11	..	..	..	1	2	1	..	..	11	..	..	..	..	4	..	..
	7-8	..	5	..	..	..	..	2	..	..	..	5	..	..	..	..	2	..	..
	8-9	2.7	30	..	1	..	4	6	..	..	..	22	..	..	..	..	4	4	..
	9-10	..	11	..	..	..	1	2	1	..	..	19	..	..	..	..	4	8	..
	10-11	..	2	..	..	..	1	..	..	..	..	2	..	..	..	..	1	..	..
	11-12	..	30	..	..	..	4	5	2	..	..	33	..	..	..	..	7	5	..
Total		8	91	2%	2%	2%	30	47	11	2	..	97+	..	..	..	2%	63%	33%	
47 Cases—Winter Series Receiving Large Doses of Cod Liver Oil from 2 weeks to 8 months of age	0-1	..	..	..	..	..	1	..	..	..	5	8	2	1	..	..	3	..	1
	1-2	12	2	5	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..
	2-3	..	..	..	..	..	1	1	..	..	..	4	..	..	..	..	2	..	..
	3-4	..	4	..	..	..	5	8	4	..	..	46	..	..	2	1	17	2	..
	4-5	10	36	2	2	1	2	1	2	..	..	19	..	..	..	..	9	..	..
	5-6	4	10	..	1	1	3	2	2	..	..	10	..	..	..	..	3	2	..
	6-7	4	14	..	1	1	..	..	..	..	..	4	..	..	..	..	..	2	..
	7-8	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Total		30+	68	14	8	8	25%	25%	17%	..	6	91	4%	2%	4%	2%	72%	12%	2%
19 Cases—Summer Series. (Control) 2 to 12 months	2-3	..	5	..	..	..	..	..	1	..	..	5	..	..	..	1	..	..	..
	3-4	..	5	..	..	..	..	1	..	..	..	5	..	..	1	..	..	..	..
	4-5	5	..	..	..	1	..	..	..	..	..	5	..	..	..	..	1	..	..
	5-6	..	5	..	..	..	..	..	1	..	..	5	..	..	..	1	..	..	..
	6-7	5	5	..	..	1	1	..	..	..	..	5	..	..	..	..	1	..	..
	7-8	..	..	..	..	..	..	..	..	..	..	5	..	..	..	..	1	..	..
	8-9	..	36	..	..	..	5	..	2	..	..	10	..	..	..	..	1	1	..
	9-10	5	5	..	..	1	1	..	..	..	..	31	..	..	3	..	2	1	..
	10-11	5	5	..	..	1	..	..	1	..	..	..	..	..	..	..	..	..	..
	11-12	..	10	..	..	..	..	1	..	1	..	26	..	..	2	..	1	2	..
Total		20+	76+	..	..	21%	30%	10%	20%	5%	..	97+	..	..	31%	10%	30%	21%	
30 Cases—Winter Series. (Control) 3 to 8 months	3	..	13	..	..	..	2	2	..	..	..	13	..	..	..	2	1	1	..
	4	..	10	..	..	..	1	2	..	..	..	13	..	..	..	2	2	..	..
	5	6	30	..	2	..	4	2	3	..	..	33	..	..	..	2	7	1	..
	6	10	10	1	1	1	1	1	1	..	..	20	..	..	..	1	5	..	..
	7	3	10	..	1	..	1	1	1	..	..	13	..	..	..	..	4	..	..
	8	3	3	..	..	1	..	..	1	..	..	6	..	..	..	1	1	..	..
Total		22	76	3%	13%	6%	30%	20%	20%	..	..	98+	..	..	..	20%	60%	6%	

* In this and in the succeeding tables, the following symbols will be used: R +—, questionable rickets; R +, mild rickets, having more than one definite rachitic manifestation; R++ and R+++, moderate rickets, having two or more rachitic manifestations; R++++, severe rickets, having marked and numerous rachitic manifestations; E, normal epiphyses; A, active rickets; B, healing rickets; C, evidence of previous rickets; ED, doubtful; AD, doubtful; BD, doubtful; CD, doubtful.

persisted and was seen as bands in the distal end of the shafts of the ulna and radius. The recent roentgenographic and histologic studies of Wimberger [5] and Eliot [6] have confirmed the rachitic nature of the roentgenographic evidence of early rickets observed. The roentgen-ray photographs of the cases reported in the protocols illustrate the changes described. The scheme [7] of recording roentgen-ray findings described by Park was utilized. Notation of the development of centers of ossification was recorded and tabulated.

BLOOD CHEMISTRY

The calcium and inorganic phosphorus of the serum was determined in twenty cases of this series, in twenty infants in the feeding ward of the hospital, and in nineteen infants with rickets who were included for comparison. The calcium was determined by Collip's modification of the Kramer-Tisdall method; the inorganic phosphorus by Tisdall's method. The determinations were made in duplicate, using 1 or 2 cc. of serum. The normal values obtained by this method on infants under 6 months being for calcium, 10.5 to 11.5 mg. per hundred cubic centimeters of serum, and for inorganic phosphorus, 5.5 to 6 mg. per hundred cubic centimeters of serum. Significant lowering of values would be below 9 for calcium and below 4.5 for inorganic phosphorus.

RESULTS OF WINTER SERIES

The results of the final observations on eighty-seven infants in the special babies' class for the prevention of rickets, are presented in detail in table 1. Here it may be seen that of the infants receiving cod liver oil, 14 per cent did not reveal any clinical evidence of rickets, 16 per cent showed only a single manifestation of rickets and 68 per cent developed two or more rachitic signs. For infants not receiving cod liver oil, 3 per cent did not reveal any clinical evidence of rickets, 19 per cent showed only one rachitic sign and 76 per cent two or more. Roentgenographic evidence of rickets was observed in 91 per cent of the infants receiving cod liver oil and in 98 per cent of the control cases. Comparing the degree of clinical rickets observed, it may be seen that no case of severe rickets was observed in either group; 42 per cent developed moderate rickets, 25 per cent mild rickets comparable to the degree of rickets observed for infants not receiving cod liver oil, namely, 40 per cent developed moderate and 30 per cent mild rickets. It is evident,

5. Wimberger, Hans: Studies of Rickets in Vienna, Medical Research Council, London, 1923, p. 95.

6. Eliot, M. M.: The Control of Rickets, J. A. M. A. **85**:656-661 (Aug. 29) 1925.

7. E, Normal epiphyses; ED, doubtful; A, active rickets; AD, doubtful; B, healing rickets; BD, doubtful; C, evidence of previous rickets; CD, doubtful.

larly by roentgen ray, for infants not receiving cod liver oil. Comparing the clinical and roentgenographic findings, it is apparent that, as a rule, the diagnosis of rickets was made earlier and more frequently by roentgen ray than by clinical examination. The diagnosis of rickets being made by roentgen ray in 4 per cent at one month and in 23 per cent by the end of two months, while by physical examination only 4 per cent were diagnosed at the end of two months. We did observe some small infants with clinical rickets to have apparently normal roentgenograms. Likewise, we observed apparently normal obese babies to show definite roentgenographic evidence of rickets.

A further analysis of table 1, showing the percentage of cases with active healing or healed rickets for all groups as seen in roentgenograms

TABLE 3.—*Distribution of Stages of Rickets (A) and Rickets Cases (B) According to Age (Schmorl)*

A

Ages, Months	Beginning		Florid		Healing		Healed		Total
	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	
2	4	100.0	..	....	..	....	..	...	4
3	12	75.0	4	25.0	..	....	..	...	16
4-6	19	57.6	7	21.2	7	21.2	..	...	33
7-9	17	34.0	23	46.0	10	20.0	..	...	50
10-12	7	9.5	45	61.7	20	27.4	1	1.4	73

B

Number of Children	Age, Months	Total Number of Cases		Rickets Absent	
		Cases	Per Cent	Cases	Per Cent
33	2-3	20	60.6	13	39.4
34	4-6	33	97.0	1	3.0
53	7-9	50	94.0	3	6.0
75	10-12	73	97.3	2	2.7

at various months, is of interest. It may be seen that the infants receiving cod liver oil showed healing rickets by the end of the fifth month in contrast with the control group, which showed activity for a longer period, not healing until seven months. Comparing the final roentgenographic evidence of active rickets observed in these infants at 5 to 8 months of age, the children in the group receiving cod liver oil showed activity in 2 per cent, compared with 26 per cent in the control group, indicating a possible controlling, curative factor operating in infants receiving cod liver oil. Roentgenograms of these infants taken in September, 1925, at from 9 to 15 months of age, showed evidence of healed rickets in almost all of the cases. The amount of healing seen seemed proportionate to the degree of previously observed rickets. The roentgenograms of infants not receiving cod liver oil seemed to show a slightly greater amount of healing. These infants, it is to be remembered, showed a slightly greater degree of rickets previously by roentgenographic examination.

then, that the majority of these infants developed a mild or moderate degree of rickets, there being little striking difference between those infants receiving and those not receiving cod liver oil.

It is also of interest to note that at the completion of the observations in May, 1925, the ages of these infants being between 5 and 9 months, the majority were apparently healthy, thriving babies. In fact, 83 per cent of the babies receiving cod liver oil and 80 per cent of the controls more than doubled their weight in five months. Except for a period, particularly during February and March, when the active symptoms of rickets were observed, the general condition and progress of the majority of the infants were good.

TABLE 2.—*Age in Months at Which Time First Evidence of Clinical and Roentgen-Ray Signs of Rickets Was Observed*

	Winter Series																			
	Cod Liver Oil (47 Cases)										Control (30 Cases)									
	Diagnosis					Roentgen-Ray Findings					Diagnosis					Roentgen-Ray Findings				
	Normal Last Seen		Clinical Rickets			E		AB		D	Normal Last Seen		Clinical Rickets			AB		E		
Age Mo.	No.	%	No.	%		No.	%	No.	%	No.	%	No.	%	No.	%		No.	%	No.	%
0–1	..	..	..	..	}	..	..	2	4	4	8	..	..	..	..	}	..	..	1	3
1–2	..	..	2	4	52	3	6	9	19	63 ..	..	..	..	5	16	56	3	10	73 ..	..
2–3	5	10	23	48	}	..	..	19	40	2	4	..	..	12	40	}	19	63	} ..	..
3–4	..	..	7	14	}	..	..	7	14	..	..	..	..	10	33	}	6	20	} ..	..
4–5	1	20	7	14	66	..	..	1	2	77 ..	..	..	..	1	3	89	1	3	93 ..	..
5–6	2	4	..	..	}	..	..	..	..	..	..	1	3	1	3	}	..	..	} ..	..
	Summer Series																			
	Cod Liver Oil (18 Cases)										Control (18 Cases)									
1–3	..	..	5	27	}	..	..	8	44	}	..	..	5	27	}	..	..	..	..	
3–4	..	..	7	38	65	..	..	7	38	82	..	..	6	33	60	..	..	..	..	
4–5	..	..	3	16		..	..	2	11		..	..	1	5		..	..	..	..	
5–6	..	..	..	..		..	..	..	..		..	..	3	16		..	..	..	..	
6–7	..	..	2	11		..	..	..	..		..	..	2	11		..	..	..	..	
7–8	..	..	1	5		..	..	..	..		..	..	1	5		..	..	..	..	

In comparing the age periods at which the first evidence of rickets was observed, both clinically and by roentgen ray, it was found that signs of clinical rickets developed at 3 months of age in 52 per cent, at 4 months in 66 per cent, while roentgenographic evidence was found at 3 months in 63 per cent and at four months in 77 per cent of infants receiving cod liver oil. Likewise, in the control group, signs of rickets developed at 3 months in 56 per cent, at 4 months in 89 per cent, and roentgenographic evidence at 3 months in 73 per cent and at 4 months in 93 per cent. Similar observations have recently been recorded by Eliot.[6] She observed 53 per cent of the cases to have roentgenographic evidence of rickets in the third and fourth months and 90 per cent positive before six months.

It is evident then that by the fourth month rickets was present in the infants of both groups showing a slightly greater incidence, particu-

An analysis of the significance and frequency of the various symptoms of rickets observed showed that, particularly in the first 3 months, cranial rickets was most frequent. If a 2 plus beading is considered a rachitic finding, it was as frequently observed as cranial rickets. A summary of the incidence of craniotabes and other associated clinical evidence of rickets is given in table 4. It may be seen here that craniotabes developed in 38 per cent of the infants receiving cod liver oil, and in 50 per cent of the controls. Craniotabes was never observed as the only symptom, and was associated with a 2 plus rosary and a 1 plus enlargement of the epiphyses, as well as marked cranial bosses and asymmetry of the head. These observations refer to the findings in the babies born in winter, when the infants were observed from birth. In the babies born in summer, covering an older age group, from 3 months to 1 year, the frequency of the rachitic symptoms was that usually described, rosary and enlarged epiphysis.

TABLE 5.—*Correlation of Signs and Symptoms of Rickets*

Age, Months	Clinical Picture	Roentgen-Ray Picture
1½ to 3½	Early rickets, development of craniotabes cranial bosses, asymmetry, head sweats, moderate rosary	Active rickets, slight hair-like threads, fraying, spreading of distal end of ulna. Osteoporosis of shaft
3½ to 5½	Moderate rickets, disappearance of craniotabes, increasing cranial bosses, square head, definite rosary, slightly enlarged epiphysis. Pallor and irritability	Active rickets with beginning healing, increased fraying and cupping, irregular shadows due to deposits of calcium in preparatory zone
6 to 15	Clinical deformities of moderate rickets, such as square head, asymmetrical head, rosary, Harrison's groove, potbelly, enlarged epiphysis, bowing	Healed rickets; contour of ulna and radius almost normal, bands of newly formed compact bone at distal ends, and along shaft

A correlation of the various clinical signs and symptoms of rickets observed, with the roentgenographic evidence of rickets present at the various age groups, is seen in table 5.

It would seem from these observations that the usually described signs of rickets, particularly those observed after 6 months of age, were found in infants with healing rickets, and that the symptoms of early rickets in infants under 6 months, particularly under 4 months of age, were found in infants with active rickets, as supported by roentgenographic evidence. It will here be noted that we did not observe any infant with severe or florid rickets in this investigation.

In considering the relation of the factors of dosage of cod liver oil, sun exposure, as well as the race, feeding and hygiene to the incidence of rickets observed in these infants, tables of the data for all groups correlating these factors were formulated. An analysis of these findings are inconclusive, none of the factors mentioned showed any significant relation to the incidence of rickets observed in these studies (see table 4). It is of interest to note, however, that a comparison of the incidence

TABLE 4.—*Summary of Incidence of Craniotabes and Other Rachitic Signs*

	Number of Cases (21) Showing Cranial Softening at Sutures at Birth to 1 Month		Number of Cases Developing Craniotabes, Month Observed and Duration		Craniotabes							Number of Cases Showing Incidence of Associated Rachitic Findings					
						Months											
	Number Developing Craniotabes	Number Did Not Develop Craniotabes	Number	Per Cent		0–1	1–2	2–3	3–4	4–5	5–6	Assymetry of Head	Craniotabes Bosses Head	Head Sweats	Rosary 2+	Epiphyses 1+	Harrison's Groove
Total number cases: 49 in winter series, 1924-1925, receiving large doses of cod liver oil. Infants were from 2 weeks of age to 8 months	9	12	19	38	1st Obs.	7	3	2	5	2	..	1	4	13	19	18	8
					Dur.	..	1	1	7	6	4		10				
36 cases, summer series 1924, receiving small doses of cod liver oil. Infants were from 1 to 3 months of age to 1 year	Not observed		14	33	1st Obs.	..	..	6	5	1	2	3	4	2	14	7	1
					Dur.	..	11	3	..	..	..						
30 cases, winter series, control group, 1924-1925	3	4	15	50	1st Obs.	2	3	5	3	2	..	6	6	8	11	11	1
					Dur.	..	..	1	3	8	3						
19 cases, summer series, control group, 1924	Not observed		3	15		..	..	1	1	..	1	..	..	..	3	..	..

and degree of rickets observed for infants receiving maximum or minimum amounts of cod liver oil showed no appreciable difference. It was also found that in the winter, over 50 per cent of the infants did not receive any direct sun exposure, and 38 per cent were given sun baths only on warm days. These percentages hold true both for infants receiving and not receiving cod liver oil. In the summer series, 25 per cent were definitely shielded from the sun, so that in winter, owing to the cold and wind, and in summer, owing to the intense heat and fear of eye-strain, a large percentage of the infants received little direct sunlight.

SIGNIFICANCE OF THE CONCENTRATION OF CALCIUM AND INORGANIC PHOSPHORUS IN THE SERUM

It is generally believed that the concentration of the inorganic phosphorus in the serum of infants with active rickets is low. Howland and Kramer [8] state that the inorganic phosphorus in the serum is regularly reduced in active rickets; that when the product of the calcium and the inorganic phosphorus concentration expressed in milligrams per hundred cubic centimeters of serum is 40 or more, rickets never results; that when the product is less than 30, rickets always results and that when the product is between 30 and 40, the degree of rickets is slight or healed.[9]

Tisdall [10] found the product of the concentration of calcium and inorganic phosphorus in the serum of infants with evidence of mild rickets (craniotabes and slightly enlarged costochondral junctions) to be 53, which is within the normal range for the method used. He raised the question whether the bony changes observed were not more of an osteoporotic nature than truly rachitic.

We have determined the concentrations of calcium and inorganic phosphorus in the serum of some of the infants showing clinical or roentgenographic evidence of early rickets. The determinations were made in March, all the infants being under 5 months of age. In table 8, the determinations for seventeen rachitic infants are presented. This table shows the concentration of calcium in eleven infants receiving cod liver oil, to average 11.4 mg. of serum and for inorganic phosphorus, 6 mg. per hundred cubic centimeters, giving a product of 68. In six infants not receiving cod liver oil, the calcium averaged 10.8 mg., and the inorganic phosphorus 6 mg. of serum per hundred cubic centimeters, giving a product of 64.

---

8. Howland, J., and Kramer, B.: Factors Concerned in the Calcification of Bone, Tr. Am. Pediat. Soc. **34**:204, 1922.

9. These figures are based on a method giving normal values for inorganic phosphorus as 5.0 mg., and for calcium 10 mg. per hundred cubic centimeters.

10. Tisdall, F. F.: The Calcium and Phosphorus Concentrations in the Serum of Infants with Mild Rickets or a Condition Simulating Mild Rickets, Am. J. Dis. Child. **24**:382 (Nov.) 1922.

TABLE 6.—*Degree of Clinical and Roentgenographic Evidence of Rickets on Final Examination for Infants of Winter Series 1924* *

Clinical Examination	Per Cent	Roentgen-Ray Examination	Per Cent
Forty-Seven Infants, Cod Liver Oil			
15 normal or doubtful	31+	3 normal	6+
32 rickets	68	1 doubtful	2
		43 rickets	91+
12 with R. 1+, mild	25	1 with A readings	2
12 with R. 2+, moderate	25+	2 with AD readings	4
8 with R. 3+, moderate	17	34 with B readings	72+
R. 4+, severe	0	6 with C readings	12
		1 with D readings	2
Thirty Infants, Control Group			
7 normal or doubtful	23+	normal or doubtful	2
23 rickets	76	rickets	98
9 with R. 1+, mild	30	8 with A readings	26
8 with R. 2+, moderate	26	20 with B readings	66
6 with R. 3+, moderate	20	2 with BD readings	6
R. 4+, severe	0		
Summer Series, 1923 †			
Thirty-Six Infants, Cod Liver Oil			
3 normal or doubtful	8	normal or doubtful	2
33 rickets	91	rickets	98
11 with R. 1+, mild	30	1 with A readings	2
17 with R. 2+, moderate	47	23 with B readings	63
4 with R. 3+, moderate	11	12 with C readings	33
1 with R. 4 , severe	2		
Nineteen Infants, Control Group			
4 normal or doubtful	21	normal or doubtful	2
15 rickets	78	rickets	98
7 with R. 1+, mild	36	6 with AD readings	31
2 with R. 2+, moderate	10	2 with A readings	10
5 with R. 3+, moderate	26	7 with B readings	36
1 with R. 4+, severe	5	4 with C readings	21

* The infants at the final examination were from 5 to 8 months of age.
† The infants at the final examination were from 8 months to 1 year of age.

TABLE 7.—*Winter Series* *

	Forty-Seven Infants on Cod Liver Oil			Thirty Cases, Control Group		
	Total per Cent	Normal ? No. Cases	Clinical Rickets, No. Cases	Total per Cent	Normal ? No. Cases	Clinical Rickets, No. Cases
Race:						
American	21	5	5	33	3	7
Irish	23	4	7	30	3	6
Italian	12	3	3	6	..	2
Greek	17	1	7	16	1	4
Colored	25	2	10	16	..	4
Feeding:						
Breast	72	12	22	66	6	14
Mixed	10	0	5	26	..	8
Artificial	17	3	5	6	1	1
Dosage:						
Maximum	53	8	17	..	..	..
½ maximum	31	5	10	..	..	..
⅓ maximum	14	2	5	..	..	..
Sun:						
3+	..	..	..	..	..	..
2+	2	..	1	6	..	2
1+	38	7	11	36	5	6
0	59	8	20	56	2	15
Open Air:						
3+	2	1	..	3	..	1
2+	17	1	7	40	5	7
1+	55	7	19	50	2	13
0	25	6	6	6	..	2
Hygiene:						
Excellent	8	1	3	13	2	2
Good	38	9	9	43	3	10
Fair	31	3	12	30	1	8
Poor	21	2	8	13	1	3

* Distribution of rickets cases according to race, hygiene and therapy.

TABLE 9.—*Concentration of the Calcium and Inorganic Phosphorus in the Serum of Infants, Aged from 1 to 3 Months, from the Feeding Ward*

Case	Age	Date of Examination	Calcium in Mg. per 100 Cc. Serum	Inorganic Phosphorus in Mg. per 100 Cc. Serum	Product	Roentgen-Ray Reading	Remarks
1	2 weeks	3/25	10.2	6.5	66.30	E	Normal
2	6 weeks	2/25	10.4	...	.....	E	Premature
3	6 weeks	3/25	....	6.3	.....	E	Premature
6	3 weeks	3/25	....	6.7	.....	E	Normal
7	3½ weeks	1/25	9.8	5.1	49.98	B_1	Normal
8	5 weeks	1/25	10.3	6.0	61.80	ED	Normal
9	4 weeks	1/25	12.0	7.5	90.0	E	Marasmus
10	2 months	3/25	10.6	4.8	50.88	E	Normal
11	2 months	3/25	12.2	6.7	81.74	B_1D	Normal
16	2 months	3/25	9.4	6.9	64.86	A_2	Convulsions
17	1 month	3/25	12.3	7.5	92.25	E	Normal
18	1 month	3/25	11.2	5.8	64.96	—	Normal
19	1 month	1/25	11.7	7.8	91.26	E	Normal
21	1 month	1/25	10.8	5.6	60.48	E	Normal
22	1 month	1/25	10.6	5.1	54.06	E	Normal
23	1 month	3/25	12.0	7.5	90.00	E	Normal
Average.....			10.2	6.3	64.26		

TABLE 10.—*Concentration of Calcium and Inorganic Phosphorus in the Serum of Infants with Rickets, Aged from 6 Months to 2 Years*

Case	Age in Mo.	Date of Examination	Calcium in Mg. per 100 Cc. Serum	Inorganic Phosphorus in Mg. per 100 Cc. Serum	Product	Findings: Rickets		Diagnosis; Remarks
						Clinical	Roentgen-Ray	
24	15	9/24	11.2	6.1	68.32	R 4. Severe	B3	Tetany (?)
25	7	3/25	12.0	3.5	42.0	R 3. Moderate	AB3	Cod liver oil (irregular)
27	24	3/25	10.8	3.9	42.12	R 5. Severe	A4B4	Marked deformity
28	14	10/24	9.0	3.4	30.60	R 4. Severe	A4.B1	Tetany
29	7	1/25	10.7	4.2	44.94	R 3. Moderate	A3.B1 - C	Tetany
30	17	1/25	7.3	3.4	24.82	R 5. Severe	A3.B4	Tetany (?)
31	5½	12/24	11.3	4.3	48.59	R 3. Moderate	A3 - C	Active rickets
33	12	12/24	9.6	4.1	39.36	R 3. Moderate	B1 - C	Active rickets
34	8 yr.	2/25	7.6	2.9	22.04	R 5. Severe	C4	Chronic richets
35	15	1/25	12.9	4.0	51.60	R 4. Severe	C4	Marked deformity
36	6	12/24	10.4	5.0	52.00	R 2. Moderate	A - B2	Cod liver oil (irregular)
37	7	2/25	7.5	5.9	44.25	R 2. Moderate	.....	Cod liver oil (irregular)
40	8	12/24	8.0	5.3	42.40	R 4. Severe	B3	Tetany
41	6	1/25	7.5	4.0	30.00	R 2. Moderate	.....	Tetany
45	4	4/25	7.6	7.8	59.28	R 3. Moderate	A1	Tetany
46	8	4/25	6.8	5.5	37.40	R 2. Moderate	A2	Tetany
Average.....			9.3	4.5	41.85			

rickets. These cases were included for comparison. The calcium concentration averaged 9.3 mg., the inorganic phosphorus 4.5 mg. per hundred cubic centimeters of serum, giving a product of 41.

Of interest and importance is the concentration of calcium and inorganic phosphorus observed in infants developing rickets, as indicated by clinical and roentgenographic findings. It will be noted that the average values obtained are within the normal range, giving a product of 68 for infants receiving cod liver oil and a product of 64 for infants not receiving cod liver oil.

TABLE 8.—*Concentration of Calcium and Inorganic Phosphorus in the Serum of Infants Developing Rickets, Aged from 2 to 5 Months*

Case	Age in Mo.	Date of Examination	Calcium in Mg. per 100 Cc. Serum	Inorganic Phosphorus in Mg. per 100 Cc. Serum	Product	Clinical Findings: Degree of Rickets	Roentgen-Ray Readings	Final Examination: Age in Mo.	Final Examination: Clinical Rickets	Final Examination: Roentgenogram
C. 20*	4	3/25	11.1	5.6	62.16	Square head Rosary 2+	BD	6	Moderate	B 1
30*	5	3/25	10.1	4.5	45.45	Square head Rosary 2+	B 2	6	Moderate	B 2
C. 4*	3	3/25	12.0	6.1	73.2	Assy. H. 2+ H. sweats 2+ Rosary 2+	AD	5	Moderate R. 3+	B 1
46*	3	3/25	11.4	5.0	57.0	Assy. H. 1+ Craniotabes 2+ Rosary 2+	B 1	5	Moderate	AB 1
36*	3½	3/25	....	6.9	.....	Cr. bosses 2+ Rosary 2+	AD	5	Moderate	CD
55*	3½	3/25	....	6.1	.....	Cr. bosses 2+ Rosary 1+	A 1	6	Mild	B 1
C. 33*	5	3/25	11.3	5.6	63.28	Cr. bosses 2+ Rosary 2+	AD	7	Moderate	B 1
C. 32*	5	3/25	11.5	6.9	79.35	Cr. bosses 2+ Craniotabes 2+ Rosary 2+	B 2	6	Moderate R. 3+	B 1
37*	5	3/25	....	6.3	.....	Normal	B 2	7	Questionable	C
75*	3	3/25	12.6	8.0	100.80	Craniotabes 2+ Assy. H. 2+ Rosary 2+	AD	5	Moderate R. 3+	B 1
C. 26*	2½	3/25	11.9	5.9	70.21	Rosary 2+ Craniotabes 2+	AD	5	Moderate	B 1
Average.....			11.4	6.0	68.40					
74#	4	3/25	12.6	7.4	93.24	Cr. bosses 2+ Rosary 2+	B 2	6	Moderate	A 1 B 1
27#	5	3/25	....	6.0	.....	Normal	A 1 B	8	Questionable	B
54#	4	3/25	11.2	6.4	71.68	Cr. bosses 2+	A 1 D	5	Moderate	B 2
84#	4	3/25	....	5.9	.....	Square head 2+ Craniotabes 2+ Rosary 2+	A 2 B 1	5	Moderate R. 3+	A 3
C. 68#†	4	3/25	9.1	5.1	46.41	Craniotabes 3+ Rosary 2+	A 3 B 1	5	Moderate	A 3
53#	4½	3/25	10.3	5.7	58.71	Cr. bosses 2+ H. sweats 1+ Rosary 2+	B 2	5	Mild	B 1
Average.....			10.8	6.0	64.80					

* Receiving cod liver oil.
\# Control group (not receiving cod liver oil).
† C indicates colored.

In table 9 are presented the determinations of calcium and inorganic phosphorus in sixteen infants under 3 months of age from the feeding ward. These infants were apparently free from rickets and were included for comparison as normal infants. The calcium averaged 10.2 mg. and for inorganic phosphorus 6.3 mg. per hundred cubic centimeters of serum, giving a product of 64.

In table 10, the determinations derived from sixteen rachitic infants, with and without tetany, are presented. The majority of these infants showed extensive clinical and roentgenographic evidence of prolonged

or cupping of the extremities of the diaphyses . . . on children with rickets between the ages of 3 months and 3 years." The majority of the children in the published cases were over 6 months of age.

These observations, of a normal inorganic phosphorus concentration in the serum of infants under 5 months of age, with early evidence of rickets in contrast with a low inorganic phosphorus concentration in the serum of infants over 6 months of age with marked rickets, suggests that, perhaps, the rickets must be marked and of some duration to show regularly a reduction of the inorganic phosphorus in the serum.

COMMENT

Any discussion of these observations on the development of rickets in infants receiving cod liver oil must be prefaced by an acknowledgment of the limitations imposed on any study undertaken in an outpatient clinic. However, practically similar limitations are in operation to a greater degree in the routine prescription of cod liver oil to babies in practice, when mothers are not supervised and do not receive the benefit of group instruction afforded in a clinic. Therefore, although open to criticism, these observations seem to have a definite value.

The incidence and degree of rickets developing in infants receiving and not receiving cod liver oil therapy did not show any striking difference. The only interesting feature was the apparent earlier healing which was observed by roentgen ray in the group receiving cod liver oil. There did not seem to be any relation between the degree of rickets observed and the amount of cod liver oil given. Comparing the incidence of clinical rickets in all the groups, the lowest was that observed in the original survey (55 per cent); the next that observed in the winter series (68 per cent); and the greatest that which occurred in the summer series (91 per cent). All of these subjects received cod liver oil under different conditions and in varying dosage. That these apparent differences are due to age and completeness of examination rather than to the influence of any other factors is indicated by the occurrence of roentgenographic evidence of rickets in practically 100 per cent for all groups.

The criteria of diagnosis of clinical rickets used in this investigation were the usually accepted ones that previously have been described. The increased incidence of cranial rickets observed, particularly craniotabes, is due to the early age period of the subjects covered in this investigation. Except for recent studies, the usual age period covered in "rickets studies" has been one ranging from 6 months to 2 years. Hess [12] states that "rickets is encountered clinically most often during the second half of the first year and the first half of the second year of life.

12. Hess, A. F.: Abt's Pediatrics **2**:910, 1923.

It has been shown by Howland and Kramer [11] that during the process of healing, whether occurring spontaneously or as the result of the administration of cod liver oil, the phosphorus content of the serum gradually rises to a normal figure and often somewhat above this. These factors were carefully considered in interpreting the normal inorganic phosphorus values obtained in these rachitic young infants, particularly those receiving cod liver oil. Although healing may have begun in some cases, either resulting from cod liver oil therapy or occurring spontaneously; clinically, the disease was apparently at its height at the time the serum was examined in March.

TABLE 11.—*Age and Number of Carpal Centers in Infants Receiving and Not Receiving Cod Liver Oil*

	Age, Months	Number of Centers				
		0	1	2	3	4
Forty-seven babies,	0-1	33	6	2	..	..
born in winter,	1-2	27	8	4	..	..
receiving cod	2-3	18	12	12	..	..
liver oil	3-4	15	2	18	..	..
	4-5	10	6	17	1	..
	5-6	7	3	19	1	..
	6-7	1	1	11	..	3
Thirty babies,	0-1	14	..	1	..	..
born in winter,	1-2	6	2	6	..	..
not receiving	2-3	11	6	9	..	..
cod liver oil	3-4	5	5	15	1	..
	4-5	6	1	13	2	..
	5-6	4	2	12	2	..
	6-7	1	1	8	..	..
Eighteen babies,	1-3	10	..	6	..	..
born in summer,	3-4	4	4	9	..	..
receiving cod	4-5	..	4	9	2	..
liver oil	5-6	2	..	14	1	..
	6-8	..	..	9	1	1
	8-10	..	..	9	2	2
	10-12	..	..	5	1	1

A further comparison of the individual determinations of inorganic phosphorus in the serum of rachitic infants revealed two striking and suggestive features. First, that those cases representing a lower age period, from 2 to 5 months, with roentgenographic evidence of early rickets, were regularly associated with a normal concentration of inorganic phosphorus and calcium in the serum. Second, that those cases representing a later age period, from 6 months to 2 years, with roentgenographic evidence of advanced and prolonged rickets, showed regularly a reduced concentration of inorganic phosphorus.

It is of interest here to note that the investigations of Howland and Kramer on calcium and phosphorus in the serum in relation to rickets were on infants "who showed unmistakable evidence of rickets . . . such as irregularity of the ends of the long bones, a fringed appearance,

11. Howland, J., and Kramer, B.: Calcium and Phosphorus in the Serum in Relation to Rickets, Am. J. Dis. Child. **22**:105 (Aug.) 1921.

TABLE 12 (Fig. 1).—*A White, Breast Fed Infant, with Roentgen-Ray Evidence of Rickets* *

Age	0-1	1-2	2-3	3-4	4-5	5-6	6-7	7	1 yr.
Month	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	March	April	Sept.
Weight	9	10-6	12-5	14-10	16-10	17-12	19	20-2	25
Condition	G.	Ex.	Ex.	Ex.	Ex.	Ex.	Ex.	Ex.	Ex.
Teeth	0	0	0	0	0	0	2	2	7
Feeding	Br.	Br.	Br.	Br.	Br.	Br.	Br.	Br.	A.
Anterior fontanel	2 × 2	2 × 2	2 × 2	1½ × 1	1½ × 1	1½ × 1	1½ × 1	1½ × 1	1
Shape of head	N	N	N	N	N	N	N	N	N
Bosses	0	0	0	0	0	0	0	0	0
Craniotabes	0	S ?	0	0	0	0	0	0	0
Head sweats	0	0	0	0	0	0	0	0	0
Rosary	0	0	0	+	+	+	+	+	++
Harrison's groove	0	0	0	0	0	0	+	+	+
Respiratory infection	0	0	0	0	0	0	0	0	0
Gastric symptoms	0	0	0	0	0	0	0	0	0
Epiphyses	0	0	0	0	0	+ —	+	+ —	+
Bowing	0	0	0	0	0	0	0	0	+
Muscular development	Good	Good	Good	Active	Active	Active	Sits	Sits	Stands
Inorganic phosphorus	0	0	0	0	0	0	6.3	0	0
Calcium	0	0	0	0	0	0	0	0	0
Roentgen-ray	E	E	E	A1	A2	B2	B3	B2	C2
Centers	0	0	0	2	4	4	4	4	4
Cod liver oil therapy, dose	½	1½	2	1 V.	1 V.	3	3	3	0
Sun	0	0	0	0	0	0	+	+	++
Outdoors	0	0	0	0	0	0	+	+	++
Hygiene	Fair	Fair	Fair	Fair	Fair	Fair	Fair	Fair	Fair

* E, Normal epiphyses; ED, doubtful; A, active rickets; AD, doubtful; B, healing rickets; BD, doubtful; C, evidence of previous rickets; CD, doubtful.

Fig. 1 (table 12).—A white, breast fed, rapidly growing baby, receiving cod-liver oil from 2 weeks of age, presented only roentgen-ray evidence of rickets. a, at 4 months, there was evidence of lipping and spreading of ulna and radius. b, at 6 months, there was evidence of rickets with healing. Note newly formed zone of preparatory calcification. c and d, roentgenogram and photograph at 7 months of age, presenting an apparently normal baby with roentgen-ray evidence of healing rickets. e, at 8 months, evidence of previous rickets. Note dense band at distal ends of shafts of ulna and radius. Contour nearly normal.

Probably it will be found that rickets, like scurvy, occurs earlier than has been supposed, and that in its milder stage it is merely latent and not subject to ordinary methods of diagnosis." The findings of roentgenographic evidence of rickets in the first 2 months, with rapid increase in the third and fourth months, would favor this hypothesis.

The correlation of the clinical and roentgenographic evidence of rickets observed in our series at the various age periods seems to indicate that active rickets is encountered most frequently in the first 6 months of life and healing rickets after 6 months. The early age incidence of the first clinical and roentgenographic evidence of rickets observed in these studies would indicate that measures of prevention or control should be instituted in the first month, particularly in babies born in winter.

The development of rickets in the babies born in winter, in whom preventative cod liver oil therapy was instituted in the first month of life under special supervision, is not easily explained, particularly in comparing the findings with those in the control group. A consideration of the age period when the greatest incidence of rickets was observed, namely, in the fourth and fifth months, suggests that the findings described may be related to the rate of growth, since the rate of growth at this age period is the most rapid in infancy. The rapid growth of the majority of the infants and their general excellent condition may, therefore, bear some relation to the findings here observed. If this disease here described is rickets, it would seem to be universal in young infants.

Of particular interest also are Schmorl's[13] statistics based on pathologic studies of bones of infants. He found on histologic examination, evidence of rickets in 60 per cent of the infants between the ages of 2 and 3 months, and in 97 per cent of the infants between the ages of 4 and 6 months. These findings are very similar to those obtained in our investigation, and lend support to the belief that the findings observed were rachitic.

A consideration of the significance of the concentration of calcium and inorganic phosphorus in the serum of infants developing rickets is of interest. Owing to the fact that the majority of published data on calcium and inorganic phosphorus in rachitic infants covered an age period of 6 months to 2 years, comparable data are not available. The cases here reported are too few in number to warrant any conclusion as to the significance of these observations, and we are, therefore, continuing this phase of the investigation. However, it may be stated that the concentration of inorganic phosphorus and calcium in the serum of infants under 5 months of age with early clinical and roentgenographic evidence of rickets, may be within the normal range.

13. Schmorl, G.: Ergebn. d. inn. Med. u. Kinderh. **4**:403, 1909.

TABLE 14 (Fig. 3).—*A White, Breast Fed Infant, with Clinical and Roentgen-Ray Signs of Rickets*

Age	0-1	1-2	2-3	3-4	4-5	5-6	6	10
Month	Nov.	Dec.	Jan.	Feb.	March	April	May	Sept.
Weight	10-10	13-13	16-4	17-11	18-9	19-2	20-10	25
Condition	Ex.	Ex.	Ex.	Ex.	Ex.	Ex.	Ex.	G.
Teeth	0	0	0	0	0	0	0	6
Feeding	Br.	Br.	Br.	Br.	Br.	Br.	Br.	A.
Anterior fontanel	0	1 × 1	2 × 2	1 × 1	1 × 1	1 × 1	1 × 1	0
Shape of head	0	0	D	Sq.+	Sq.++	Sq.++	Assy.Sq.	Sq.
Bosses	0	+ —	P++	P++	P++	P++	P++F++	P+++
Craniotabes	0	0	++	+++	++	+	0	0
Head sweats	0	0	+	+	+	+	0	0
Rosary	0	+	++	+++	+++	+++	++	+++
Harrison's groove	0	0	0	0	0	0	++	++
Respiratory infection	0	+	0	0	0	0	0	0
Gastric infection	0	0	0	0	0	0	C	0
Epiphyses	0	+ —	+	++	++	++	++	++
Bowing	0	0	+	++	++	++	++	++
Muscular development	0	Active	Active	Sits	Sits	Sits	Sits	Sits
Inorganic phosphorus	0	0	0	0	5.9	0	0	0
Roentgen ray	E	E	A D	A2	A3	AB2	B2	C2
Centers	1 —	2 +	2 +	2 +	2 +	2 +	2	0
Cod liver oil therapy	None	None	None	None	None	None	None	None
Alpine light	0	0	0	0	0	Alp.L.	Alp.L.	Alp.L.
Sun	0	0	+ —	+ —	+ —	+ —	+ —	3 +
Outdoors	+	+	++	++	+ —	++	++	3 +
Hygiene	Good	Good	Good	Good	Good	Good	Good	Good

Fig. 3 (table 14).—This was a white, breast fed, rapidly growing infant, who developed rickets. The inorganic phosphorus was 5.9 mg., with clinical and roentgen-ray evidence of rickets. a, at 3 weeks, the bones were normal. b, at 2 months, spreading and fraying of the ulna and lipping of radius were noted. c, at 3 months, the rickets was progressing; the shadow of a newly formed zone of preparatory calcification may be seen. d, at 5 months, the infant was a fat, pale baby, with a square head, residual craniotabes, rosary and Harrison's groove. e, changes were progressing; the healing is more evident at the distal end of the ulna and radius. Note the osteophyte layer along the shafts. f, at 6 months, there was healing rickets and a nearly normal contour.

TABLE 13 (Fig. 2).—*This Baby, Irish, Developed Clinical Rickets*

Age	0-1	1-2	2-3	3-4	4-5	5-6	6	10
Month	Dec.	Jan.	Feb.	March	April	May	June.	Sept.
Weight	7-12	8-12	9-6	10-9	12	13-6	15-2	18
Condition	Ex.	Ex.	F.	F.	F.	G.	G.	G.
Teeth	—	—	—	—	—	2	2	8
Feedings	Br.	M.	A.	A.	A.	A	A.	A.
Anterior fontanel	—	2 × 2	2 × 2	2 × 2	2 × 2	2 × 2	1 × 1	1
Shape of head	N	N	Assy.+	Assy.++	Sq.++	Sq.	Assy.Sq.	Sq.
Bosses	—	—	F+P+	F+P++	F+P++	F+P+	F+P+	++
Craniotabes	S ?	0	0	++	++	++	0	0
Head sweats	+	+	+	++	+	+	0	0
Rosary	+—	+—	+—	++	++	+	++	++
Harrison's groove	0	0	0	0	0	0	+	++
Respiratory infection	0	0	0	0	+	0	0	0
Gastric symptoms	0	0	C	C	0	0	0	0
Epiphyses	+—	+—	+—	+	+	+	+	++
Bowing	0	+—	+—	+—	+—	+	+	++
Muscular development	Active	Active	Active	Active	Active	Flabby	Active	Sits
Calcium	—	—	—	12	—	—	—	—
Inorganic phosphorus	—	—	—	8.0	—	—	—	—
Roentgen ray	ED	E	E	AD	A1	B1	B1	C1
Centers	1—	1—	1	1	1	2	2	0
Therapy, cod liver oil dose	½	½	3	3	3	3	2	—
Sun	+—	+—	+—	+	+	+	+	+
Outdoors	+—	+—	+—	+	+	++	++	++
Hygiene	Fair	Fair	Fair	Fair	Fair	Fair	Fair	Fair

Fig. 2 (table 13).—A white, Irish, artificially fed baby, receiving cod-liver oil from 2 weeks of age, developed 3 + clinical rickets with slight roentgen-ray findings. a, at 2½ months, there was no evidence of rickets. b, at 3½ months, there was possible slight evidence of spreading at the distal end of the ulna. The bone structure was coarse. c, at 4 months, there was evidence of early rickets. Note fraying and slight cupping of the metaphyseal margin of the ulna. d, at 6 months, the rickets was healing. e, at 5 months, the infant weighed 13 pounds, and was pale and flabby, with residual craniotabes and asymmetry of the head.

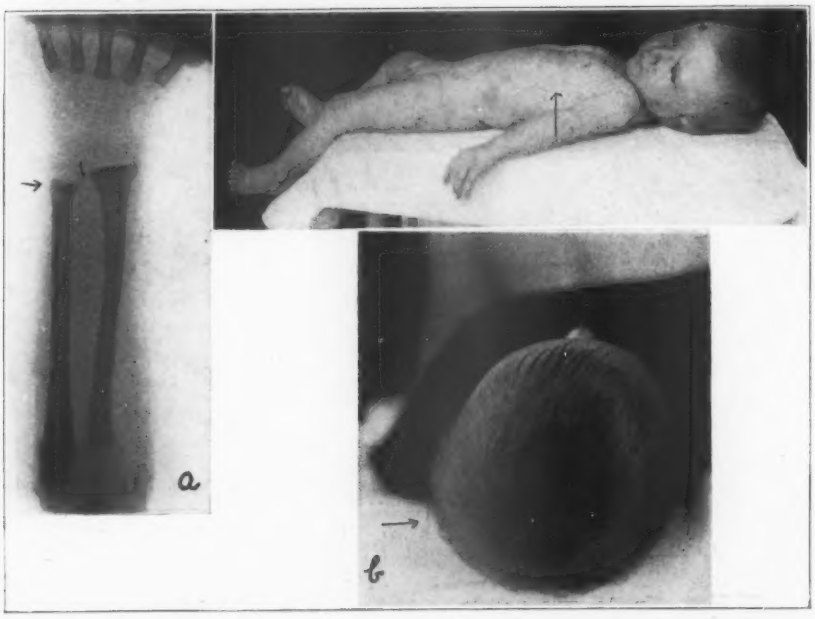


Fig. 5.—A typical case of early rickets. This infant was white, artificially fed, and did not receive cod liver oil. a, at 3 months, the distal metaphyseal margin of the ulna was ill defined, slightly frayed and spread. Concomitant physical findings present were: craniotabes, cranial bosses, asymmetry and 2+ beading with head sweats and irritability. b, at 4 months, the infant was a rachitic, typically pale baby.

TABLE 15 (Fig. 4).—*A Colored, Breast Fed Infant, Who Developed Rickets (Case 68)*

Age	0-1	1-2	2-3	3-4	4-5	5-6	9
Month	Dec.	Jan.	Feb.	March	April	April	Sept.
Weight	5-8	8-14	11-12	13-2	14-2	14-9	17-¾
Condition	G.	G.	G.	G.	G.	Ex.	G.
Teeth	0	0	0	0	0	0	0
Feeding	Br.	Br.	Br.	Br.	Br.	Br.	M.
Anterior fontanel	1½ × 2	1½ × 1½	3 × 2	3 × 2	3 × 2	3	0
Shape of head	0	Assy.	Assy.	Assy.	Assy.	Assy.	Assy.
Bosses	0	0	P++F++	P+ F+	P+ F+	P+ F+	++
Craniotabes	0	0	+++	+++	+++	+++	0
Head sweats	0	0	0	+	+	0	0
Rosary	0	+	+	++	++	++	++
Harrison's groove	0	0	0	0	0	0	++
Respiratory infection	0	0	+	+	0	0	+
Gastric symptoms	0	0	0	0	0	0	C
Epiphyses	0	0	+	+	+	+	++
Bowing	0	+	++	++	+	+	+
Muscular development	Active	Active	Active	Active	Active	Active	Sits
Calcium	0	0	0	9.1	0	0	0
Inorganic phosphorus	0	0	0	5.1	0	0	0
Roentgen ray	E D	A D	A1	A2	A3 B1	A3 B2	B3 C2
Centers	0	0	0	0	0	0	0
Cod liver oil therapy, dose	None	None	None	None	None	C.L.O.	C.L.O.
Sun	0	0	0	0	0	++	+
Outdoors	0	0	+	+	+	++	+
Hygiene	Good	Good	Good	Good	Good	Good	Good

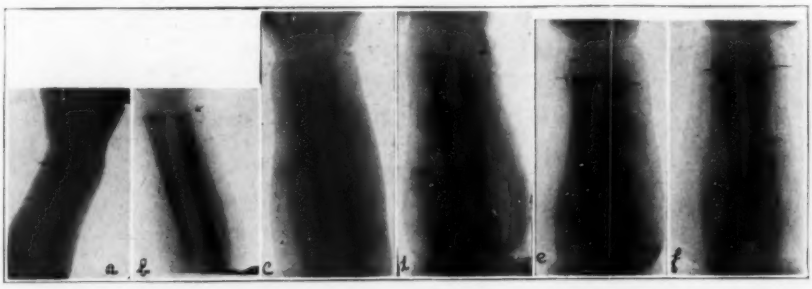


Fig. 4 (table 15).—A colored, breast fed infant, developed rickets. No cod-liver oil had been given. The inorganic phosphorus was 5.1. a, doubtful normal; b, doubtful evidence of early rickets. Note slight fraying of the ulna. c, definite evidence of early rickets. Note hair-like threads from the left margin of the metaphysis of the ulna. d, rickets was progressing. Note irregular contour of the ulna and the radius, cupping of the ulna and osteoporosis of shafts. e, rickets was progressing. Evidence of healing; f, healing progressing. Note dense bands at distal ends of ulna and radius.

TABLE 18.—*Findings in a Colored Infant (Case 26)*

Age	0-1	1-2	2-3	3-4	4-5	5-0
Month	Jan.	Feb.	March	April	May	May
Weight	7	9-9	11-12	12-5	11-4	11-5
Condition	G.	G.	F.	F.	F.	F.
Teeth	0	0	0	0	0	0
Feeding	Br.	Br.	Br.	Br.	Br.	Br.
Anterior fontanel	P.	2 × 3	2 × 3	2 × 3	2 × 3	2 × 3
Shape of head	N.	N.	N.	N.	N.	N.
Bosses	—	—	+	+	+	+
Craniotabes	0	0	++	++	+	+
Head sweats	0	0	0	0	0	0
Rosary	—	+	++	++	++	++
Harrison's groove	—	—	—	+	+	+
Respiratory infection	0	0	+	+	+	+
Gastric infection	0	0	0	0	0	0
Epiphyses	0	+	+	+	+	+
Bowing	0	+	+ —	+ —	+ —	0
Muscular development	Poor	Poor	Poor	Poor	Poor	Poor
Calcium	0	0	11.9	0	0	0
Inorganic phosphorus	0	0	5.9	0	0	0
Roentgen-ray	E	A1 D	A D	E D	B1 D	B1
Centers	0	0	0	0	0	1 +
Cod liver oil therapy, dose	1	2 V.1	3 V.1	3 V.1	3 V.1	3 V.2
Sun	0	0	0	0	+	0
Outdoors	+	+	+	+	++	0
Hygiene	F.	F.	F.	F.	F.	F.

TABLE 19.—*Findings in a White, American Infant (Case 46)*

Age	0-1	1-2	2-3	3-4	4-5	5-6	6
Month	Dec.	Jan.	Feb.	March	April	May	June
Weight	8-4	9-11	11	12-8	13-8	14	14-8
Condition	G.	Ex.	Ex.	Ex.	Ex.	Ex.	Ex.
Teeth	0	0	0	0	0	0	0
Feeding	Br.	Br.	Br.	Br.	M.	M.	M.
Anterior fontanel	2 × 2½	2 × 2	2 × 2	1 × 1	2 × 1	1 × 1	1 × 1
Shape of head	N.	N.	N.	N.	Assy.	Assy.	Assy.
Bosses	—	—	P+	P++	P++	P++	P++
Craniotabes	S	0	0	+	++	++	0
Head sweats	0	0	0	+	+	0	0
Respiratory infection	0	0	0	0	0	0	0
Gastric infection	C	C	C	C	C	C	C
Rosary	0	+	++	+	+	+	++
Harrison's groove	0	0	0	0	0	0	+
Epiphyses	0	0	0	+	+	+	+
Bowing	0	+ —	+ —	+ —	+ —	0	0
Muscular development	Good	Good	Active	Active	Active	Active	Active
Calcium	0	0	0	11.4	0	0	0
Inorganic phosphorus	0	0	0	5.0	0	0	0
Roentgen ray	E	E D	A1 D	B1	A1 B1	A1	A1 B1
Centers	0	0	1 —	1	1	1 —	2 —
Cod liver oil therapy, dose	½	1 ?	1 ?	2	3	3	3
Sun	0	0	0	0	+	+	+
Outdoors	0	0	+	+	+	+	+
Hygiene	F.	F.	F.	F.	F.	F.	F.

TABLE 16.—*A Colored, Breast Fed Infant, Who Had Received Cod Liver Oil from the Age of 2 Weeks, Developed Moderate Clinical Rickets with Slight Roentgen-Ray Evidence. At 3 Months of Age, the Contour of the Ulna Was Ill Defined. At 5 Months the Rickets Was Healing, and the Contour Was Nearly Normal (Case 4)*

Age	0-1	1-2	2-3	3-4	4-5	5
Month	Dec.	Jan.	Feb.	March	April	May
Weight	8	7-6	0	10-5	13-1	15-4
Teeth	0	0	0	0	0	0
Feeding	Br.	Br.	Br.	Br.	Br.	Br.
Anterior fontanel	P.	3 × 3	3 × 3	3 × 3	3 × 3	3 × 3
Shape of head	N.	N.	N.	Assy.	Assy.	Assy.
Bosses	0	0	P+	P++	P++	P++
Craniotabes	S	S	0	0	++	+
Head sweats	0	0	0	++	++	+++
Rosary	+−	+	+−	++	++	++
Harrison's groove	0	0	0	0	++	++
Respiratory infection	0	0	0	+	++	++
Gastric infection	0	0	0	0	C	C
Epiphyses	0	1 +	+−	+−	+	+
Bowing	0	0	0	+	+	+
Muscular development	Poor	Poor	Poor	Flabby	Flabby	Flabby
Calcium	0	0	0	12.0	0	0
Inorganic phosphorus	0	0	0	6.1	0	0
Roentgen-ray	E	E D	E D	A	B	B
Centers	0	0	1	2	2	2
Cod liver oil therapy, dose	½	1	3	3	3	3
Sun	0	0	0	0	0	0
Outdoors	+	+	+	+	+	+
Hygiene	Good	Good	Good	Good	Good	Good

TABLE 17.—*A Colored, Breast Fed Infant, Who Received Cod Liver Oil from the Age of 2 Weeks, Developed Moderate Rickets by Clinical and Roentgen-Ray Examination. At the Age of 2½ Months, the Contour of the Ulna Was Irregular. Slight Cupping. At 4 Months the Contour Was Nearly Normal, and the Metaphyseal Margins Were Sharply Defined (Case 20)*

Age	0-1	1-2	2-3	3-4	4-5	5-6	6	10
Month	Nov.	Dec.	Jan.	Feb.	March	April	May	Sept.
Weight	7-7	9-4	9-9	11-14	13-6	14-8	15-2	19
Condition	Ex.	Ex.	Ex.	Ex.	Ex.	Ex.	Ex.	Ex.
Teeth	0	0	0	0	0	0	0	0
Feeding	Br.	Br.	Br.	Br.	Br.	Br.	Br.	M.
Anterior fontanel	P.	2 × 1¾	2 × 1¾	3 × 2	3 × 2	3 × 2	3 × 2	2
Shape of head	N.	N.	N.	N.	N.	Sq.	Assy.	Assy.Sq.
Bosses	0	0	P++	P+	P+	P++	P+ F+	+
Craniotabes	0	S	0	0	0	0	0	0
Head sweats	0	0	0	0	0	0	0	0
Rosary	0	++	++	++	++	++	++	++
Harrison's groove	0	0	0	0	0	0	0	0
Respiratory infection	0	+	+	0	0	0	0	0
Gastric infection	0	0	0	0	0	0	0	0
Epiphyses	0	0	0	0	+	+	+	+
Bowing	0	0	+	+	+	+	+	+
Muscular development	Good	Good	Good	Good	Active	Active	Active	Active
Calcium	0	0	0	0	11.1	0	0	0
Inorganic phosphorus	0	0	0	0	5.6	0	0	0
Roentgen ray	E D	E D	A D	A B	B	B	B	C
Centers	0	0	1	2	2	2	2	0
Cod liver oil therapy, dose	½	½	½	3	3	3	3	3
Sun	0	0	+	+	+	+	+	+
Outdoors	0	0	+	++	++	++	++	++
Hygiene	Good	Good	Good	Good	Good	Good	Good	Good

TABLE 22.—*Findings in an Infant, Irish (Case 27)*

Age	0-1	1-2	2-3	3-4	4-5	5-6	6-7	8	1 yr.
Month	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	March	May	Sept.
Weight	9-4	10-13	12-10	13-8	14-12	15-6	15-10	16-7	19-
Condition	Ex.	Ex.	Ex.	Ex.	Ex.	Ex.	Ex.	Ex.	Ex.
Teeth	0	0	0	0	0	2	0	4	10
Feeding	Br.	Br.	Br.	Br.	Br.	Br.	Br.	Br.	M.
Anterior fontanel	1½	1½	1½	1½	3 × 2	2 × 1	2 × 1	2 × 1	1
Shape of head	N — +	N + —	N + —	N + —	N + —	N + —	N +	N +	0
Bosses	0	0	0	0	0	0	0	0	F ++
Craniotabes	0	0	0	0	0	0	?	0	0
Head sweats	0	0	0	0	0	0	0	0	0
Rosary	+ —	+ —	+ —	++	++	++	++	++	++
Harrison's groove	0	0	0	0	0	0	0	+	+++
Respiratory infection	+	0	0	0	0	0	0	0	0
Gastric infection	C	0	0	0	0	0	0	0	0
Epiphyses	—	—	—	—	+ —	+	+	++	++
Bowing	0	0	0	0	0	+	+	+	+
Muscular development	Active	Active	Active	Active	Active	Active	Sits	Sits	Stands
Calcium	0	0	0	0	0	0	0	0	0
Inorganic phosphorus	0	0	0	0v	0	0	6.8	0	0
Roentgen ray	E	E	E	E	A1D	A1D	B2	B1	C
Centers	0	0	0	0	1 —	2 —	2	2	0
Massage, no cod liver oil	1	1	1	1	1	3	3	3	0
Sun	—	—	—	—	—	—	—	—	Tan
Outdoors	+	+	+	+	+	++	++	++	Tan
Hygiene	Bad	Bad	Bad	Bad	Bad	Bad	Bad	Bad	Bad

TABLE 23.—*Findings in an American Infant (Case 74)*

Age	0-1	1-2	2-3	3-4	4-5	5-6	6	9½
Month	Nov.	Dec.	Jan.	Feb.	March	April	May	Sept.
Weight	7-8	0	0	10-10	11-12	12-5	13-14	17
Condition	G.	G.	G.	G.	G.	G.	G.	G.
Teeth	0	0	0	0	0	0	0	2
Feeding	Br.	Br.	Br.	Br.	A.	A.	A.	A.
Anterior fontanel	—	3 × 2	3 × 2	3 × 2	2 × 1	2 × 1	2 × 1	1
Shape of head	—	N	N	Sq.+	Sq.+	Sq.+	Assy. Sq.++	Sq.
Bosses	—	0	0	P+ F+	P++	P+ F+	P+ F++	3 +
Craniotabes	—	0	0	+	+	0	0	0
Head sweats	—	0	0	0	0	0	0	0
Rosary	—	—	—	+	++	++	+	+
Harrison's groove	—	0	0	0	0	0	+	+
Respiratory infection	—	0	0	++	++	0	0	+
Gastric infection	—	0	0	0	0	0	0	0
Epiphyses	—	—	—	+	+ —	+ —	+	+
Bowing	—	—	—	+	+ —	+ —	+ —	+
Muscular development	—	Good	Active	Active	Active	Active	Sits	Stands
Calcium	0	0	0	0	12.6	0	0	0
Inorganic phosphorus	0	0	0	0	7.4	0	0	0
Roentgen ray	0	E	E	A1	A2B1	B2	B2	C
Centers	0	0	0	0	0	0	0	0
Massage, no cod liver oil	0	1	1	1	1	11	1	0
Sun	0	+ —	+ —	+ —	+ —	+	+++	+
Outdoors	0	+	+	+	+	+	+++	+
Hygiene	Good	Good	Good	Good	Good	Good	Good	Good

TABLE 20.—*A White, American Infant, Who Gained Slowly. The Findings in This Case Showed Little Evidence of Rickets. At 2 Weeks, the Bones Were Normal. At 3 Months, the Metaphyseal Margins Were Slightly Frayed. At 5 Months, the Rickets Was Healing (Case 36)*

Age	0-1	1-2	2-3	3-4	4-5	5-6	6
Month	Dec.	Jan.	Feb.	March	April	April	May
Weight	5-12	7-1	9-14	10-13	11-2	11-15	13
Condition	G.	G.	G.	G.	F.	F.	G.
Teeth	0	0	0	0	0	0	0
Feeding	Br.	M.	M.	A.	A.	A.	A.
Anterior fontanel	1½ × 1	1½ × 1	1½ × 1	2 × 1	2 × 1	2 × 1	2 × 1
Shape of head	N.	N.	N	N.	N.	Small	0
Bosses	0	0	F+	F+	F++ P++	F+ P+	P+
Craniotabes	S ?	0	+	+	++	0	0
Head sweats	0	0	0	+	0	0	0
Rosary	++	+	++	++	++	++	+
Harrison's groove	0	0	0	0	0	0	0
Respiratory infection	0	0	0	0	0	0	0
Gastric infection	0	0	C	C	0	0	0
Epiphyses	0	0	+ —	+	+	+	+
Bowing	0	0	0	0	0	0	+
Muscular development	Good	Active	Active	Active	Active	Active	A B
Calcium	0	0	0	0	0	0	0
Inorganic phosphorus	0	0	0	6.9	0	0	0
Roentgen ray	E	E	A D	A D	B D	A D	C
Centers	0	0	0	0	0	1 —	1
Cod liver oil therapy, dose	1	2	2½	3	3	3	3
Sun	0	0	+	+	+	+	+
Outdoors	+	+	++	++	++	++	++
Hygiene	P.	P.	G.	G.	G.	G.	G.

TABLE 21.—*A Colored, Breast Fed Infant, Who Received Cod Liver Oil from 2 Weeks of Age, Developed Moderate Rickets (Case 32)*

Age	0-1	1-2	2-3	3-4	4-5	5-6	6
Month	Oct.	Nov.	Dec.	Jan.	Feb.	March	April
Weight	8-10	11-8	12-9	15-12	17	18-15	20
Condition	G.	G.	G.	G.	Ex.	Ex.	Ex.
Teeth	0	0	0	0	0	0	0
Feeding	Br.	Br.	Br.	Br.	Br.	Br.	M.
Anterior fontanel	3 × 2	3 × 2	3 × 2	3 × 2	3 × 2	3 × 2	2
Shape of head	N.	N.	N.	Sq.	Sq.	Sq.	Sq.
Bosses	0	+ —	+ —	P+	P+ F+	P+ F+	++
Craniotabes	0	0	+	++	++	++	+
Head sweats	0	+	+	0	0	0	0
Rosary	0	++	++	++	+++	++	++
Harrison's groove	0	0	0	+	+	+	+
Respiratory infection	+	0	0	0	+	0	0
Gastric infection	C	0	0	0	0	0	0
Epiphyses	0	+	+	+	++	++	++
Bowing	0	0	0	+ —	+ —	+ —	+
Muscular development	Good	Good	Good	Active	Active	Active	Active
Calcium	0	0	0	0	0	11.5	0
Inorganic phosphorus	0	0	0	0	0	6.9	0
Roentgen ray	A D	A D	B2	B2	A2 B2	B3	B3
Centers	1	2½	3	5	6	6	7
Cod liver oil therapy, dose	½	½	½	1½	3	3	3
Sun	0	0	0	0	0	0	+
Outdoors	+ —	+ —	+ —	+ —	+ —	+ —	+
Hygiene	P.	P.	P.	P.	P.	P.	P.

ETIOLOGY AND HEALING PROCESS OF DUODENAL ULCER IN MELENA NEONATORUM *

ROGER L. J. KENNEDY, M.D.

ROCHESTER, MINN.

Examination of the literature dealing with true melena neonatorum shows that there is no agreement in regard to its etiology. It has long been known that duodenal ulcers may be found in infants who have died from melena. Shukowsky,[1] in 1907, estimated that ulcers of the gastro-intestinal tract, including the esophagus, stomach, duodenum and lower intestine, have been demonstrated in 45 per cent. of such infants. Theile[2] found records of sixty-four cases of ulcer of the gastro-intestinal tract occurring with melena neonatorum; thirty-one were in the duodenum and twenty-nine in the stomach. He does not give the percentage of cases of melena neonatorum without lesions.

Undoubtedly, duodenal ulcer is much more common than has generally been accepted, and more common than Shukowsky's estimate of 45 per cent. As I have pointed out,[3] they are easily overlooked at necropsy because they may be very small, and obscured by blood, mucus or fibrin. One of the cases formerly reported, and the case reported here, were of this type. In one case the duodenum was free from gross lesions, and in the other a small submucous hemorrhage was mistaken for the ulcer. The ease with which such ulcers are overlooked has led to the belief that in about half the cases, melena neonatorum is due to oozing from the mucosa of the gastro-intestinal tract, although the nature of the oozing that will produce from eight to ten bloody stools in twenty-four hours has not been adequately explained. The point to be emphasized is that duodenal or gastric ulcer should be suspected in every case of melena neonatorum, and, if it is not seen grossly at necropsy, its absence should be proved by the examination of microscopic sections of the entire duodenum or stomach. The case reported here demanded such detailed study before the lesion could be demonstrated conclusively.

---

* Received for publication, Nov. 3, 1925.

* From the Section on Pediatrics, Mayo Clinic.

1. Shukowsky, W. P.: Melaena Neonatorum, Magendarmblutungen bei Neugeborenen, Arch. f. Kinderh. **45**:321-373, 1907.

2. Theile, Paul: Ueber Geschwürsbildungen des Gastroduodenaltractus im Kindesalter, Ergebn. d. inn. Med. u. Kinderh. **16**:302-383, 1919.

3. Kennedy, R. L. J.: Duodenal Ulcer and Melena Neonatorum, Am. J. Dis. Child. **28**:694-699 (Dec.) 1924.

SUMMARY

1. A study of infants, aged from 1 to 3 months, born in the spring and summer of 1924, receiving graduated doses of one half to one and one half teaspoonfuls of a biologically tested cod liver oil, revealed the development of clinical rickets in 91 per cent of the subjects.

2. A more intensive study of forty-seven infants, aged from 2 weeks, born in the winter of 1925, receiving daily doses of one, two and three teaspoonfuls of biologically tested cod liver oil, showed the development of clinical rickets in 68 per cent of the cases, as compared with 76 per cent of the control series of thirty cases.

3. Ninety-seven per cent of infants born in the summer, and 91 per cent of infants born in the winter who received cod liver oil showed roentgenographic evidence of rickets.

4. Ninety-seven per cent of the infants born in the summer, and 98 per cent of infants born in the winter who did not receive cod liver oil, showed roentgenographic evidence of rickets.

5. Rickets was observed earlier by roentgen ray than by clinical examination, being observed in 4 per cent at 1 month and in 23 per cent at 2 months of age, compared with a total of 4 per cent at 2 months by clinical examination alone.

6. By the fourth month, rickets was present in the majority of infants of both groups.

7. The early age incidence of the development of rickets observed, indicates the necessity for measures of prevention or control to be instituted in the first month, particularly for babies born in winter.

8. The correlation of the clinical and roentgenographic evidence of rickets observed at the various age periods in this investigation indicated that active rickets is encountered most frequently in the first 6 months of life, and healing rickets after 6 months.

9. There did not seem to be any relation between the degree of rickets observed and the amount of cod liver oil received.

10. The concentration of calcium and inorganic phosphorus in the serum of infants under 5 months of age, with early clinical and roentgenographic evidence of rickets, was found to be within the normal range.

11. A comparison of the degree and incidence of rickets observed in infants receiving and not receiving cod liver oil did not reveal any striking difference.

12. Infants receiving cod liver oil showed rickets that healed earlier than that of the control series.

13. The nature of the relation of cod liver oil therapy to the development of rickets, as observed in these studies, would seem to be one of control rather than of prevention.

121 East Sixtieth Street.

tract from the pylorus to the anus. Permission to examine the cranial contents could not be obtained, and the gross examination, including that of the gastro-intestinal tract, was otherwise negative except for the marked pallor of all the organs and tissues of the body. A small dark area, about 2 mm. in diameter, seen on the wall of the duodenum just distal to the pylorus, was thought to be an ulcer. The stomach and slightly more than the first portion of the duodenum were fixed in Kaiserling solution. This portion of the duodenum and a small portion of the stomach were sectioned serially and examined microscopically. The duodenum was normal save at two points. The small dark area proved to be a small hemorrhage beneath the mucosa. On the duodenal side of the pyloric fold of the mucosa was an ulcer (Fig. 1) which extended through the muscularis mucosa. It was made up of a mass of fibrin covering the crater area, the base of which was invaded by actively proliferating, young connective tissue cells and fibers. In the deeper portions of this and in the adjacent muscularis, there was a slight infiltration by polymorphonuclear and small round cells; in many

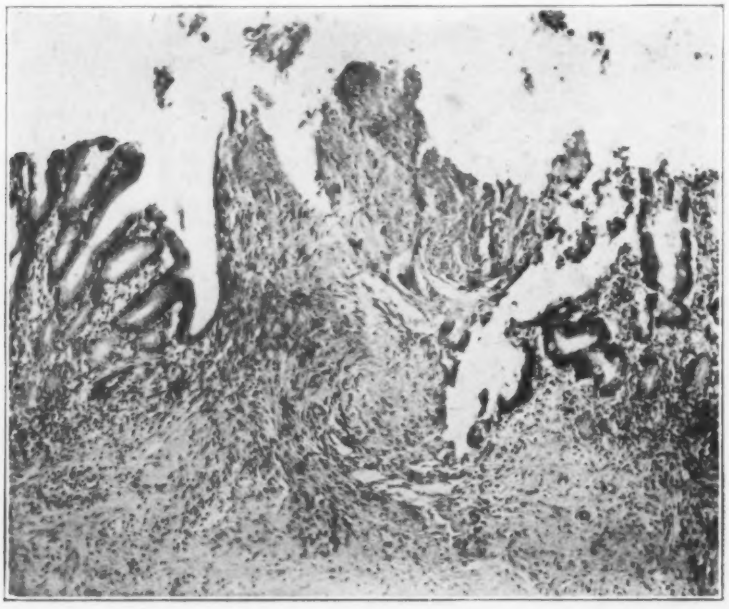


Fig. 2.—Section through center of ulcer. Some of the organizing fibrin has rubbed off from the top of the specimen. Note the fibrin, the connective tissue proliferation and cellular reaction. (× 60.)

instances the polymorphonuclear cells were eosinophilic in type. The epithelium of the glands of Brunner and the glands of the duodenal mucosa, which at certain points were involved in the destructive process, showed evidence of proliferation in an effort at repair. At the edges of the ulcer there was a definite downgrowth of the epithelial cells of the mucous membrane. Where these cells met the granulation tissue filling the crater of the ulcer, they were cuboidal and extended over the sides of the granulating mass. Still further from the intact mucosa, the cells were shorter, and finally flat (Fig. 2). At the edges of the ulcer, tangential sections showed a layer of flat epithelial cells covering the granulation tissue (Fig. 3).

The situation of the ulcer in the duodenum, proximal to the papilla of Vater, coincides with that of ulcers recorded as having been found associated with

REPORT OF A CASE

A girl, aged 3 days, was brought to the Mayo Clinic from a nearby town because of reddish-brown stools, which had been passed since the previous day. The mother was a primipara, aged 19; the father was aged 45. Delivery occurred at term, after a normal pregnancy, and was comparatively easy and spontaneous. Two hours after delivery, oozing from the umbilical stump began, although the ligature appeared to be intact. Repeated ligation did not control the oozing. On the second day, there were signs of loss of blood and the attending physician gave physiologic sodium chlorid solution subcutaneously. About this time, the infant began to pass dark reddish-brown stools, and vomited a small amount of mucus with reddish-brown streaks. Stools of this color were passed three or four times during the next twenty-four hours, and the baby became progressively paler.

The coagulation time of the blood was nine minutes and the bleeding time was three hours. The puncture wound oozed a small amount of blood during

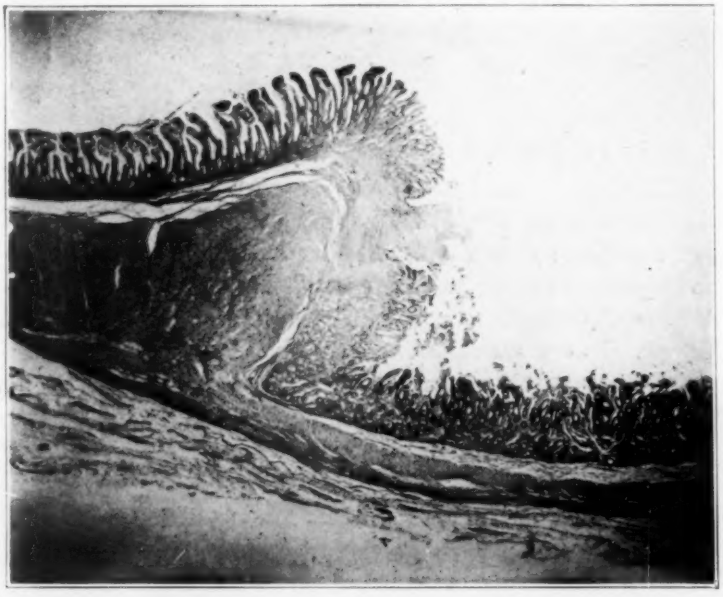


Fig. 1.—Section through pylorus and parts of stomach and duodenum. The ulcer is shown on the pyloric fold of mucosa. The destructive process extends to the muscular layer of the pylorus. (× 12.)

that period. A sinus transfusion was attempted but, on account of the overlapping of the cranial bones, was unsuccessful, and 20 c.c. of whole blood was injected intramuscularly at 5:00 p. m. At 9:00 p. m., 40 c.c. of whole blood was injected in a similar manner. At this time it was noted that the hemorrhage from the umbilical stump had ceased. During the next two days there were about twelve stools, which changed gradually from reddish-black to brown, and then to bright red. On the second day the hemorrhage from the umbilical stump began again, and 40 c.c. of blood was given intraperitoneally, and 10 c.c. intramuscularly. Another attempt at sinus transfusion was unsuccessful. The pallor rapidly became extreme, and the child died on the fifth day.

Necropsy.—This showed several small scattered hemorrhages beneath the pleurae, and a large quantity of dark brown blood filling the gastro-intestinal

evidence show that the initial lesion begins to heal almost coincidently with its formation, and that the process of healing in this case, up to the point at which the ulcer was covered by epithelium and the granulation tissue was well organized, occupied not more than four or five days.

Mann believes that under favorable conditions duodenal ulcers often occur which heal so rapidly and completely as to leave no evidence of their presence on gross examination, and that only careful histologic study, and the knowledge gathered from experimental observations can enable one to detect the remains of one of these healed lesions. He suggests that the ulcer in this case might have healed so completely as to make its recognition impossible if the infant had lived for two or three days longer.

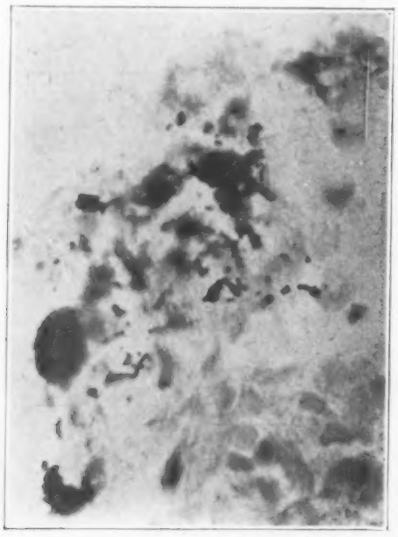


Fig. 4.—Diplococci and short chains in sloughing tissue of ulcer shown in Figures 1 and 2. (Modified gram, × 1,000.)

Similar attempts at healing displayed by the glands of Brunner have been noted by Helmholz,[5] who found that, in a case in which these glands were involved in the ulceration, the epithelium of the glands was quite changed. The cells had become lower and flatter, had grown away from their original site, and extended in the form of an unbroken membrane for a considerable distance into the tissue, which filled the crater of the ulcer.

Not only has the etiology of melena neonatorum not been determined, but the cause of peptic ulcers in the new-born has been the subject of

5. Helmholz, H. F.: Die Regeneration des Darmepithels von den Brunnerschen Drüsen in oberflächlichen Duodenalgeschwüren, Virchows Arch. f. path. Anat. **201**:243-245, 1910.

melena. The fact that it was on the pyloric fold of the mucosa, rather than on the posterior or anterior wall, is unusual, although it was within the usual ulcer-bearing portion of the duodenum, that is, between the pylorus and the papilla of Vater.

The ulcer was small; the absence of a visible crater, and the situation account for its being overlooked at necropsy. Allowing the shrinkage due to fixing the tissue, the size was estimated at 2 mm. It might have been found had the crater not been obliterated by granulation tissue, which gave an unbroken appearance to the mucosa. Clinically, it would appear that the ulcer was probably not present before birth; pathologically, the time of onset could not be determined. It is, however, a favorable point of comparison between the experimentally produced duodenal ulcer and the early healing ulcer in man. The similarity between some of the lesions produced experimentally by Mann [4] and the lesion described here is most striking. The site, the pathologic changes, and the rapidity of healing were the same. Both sources of

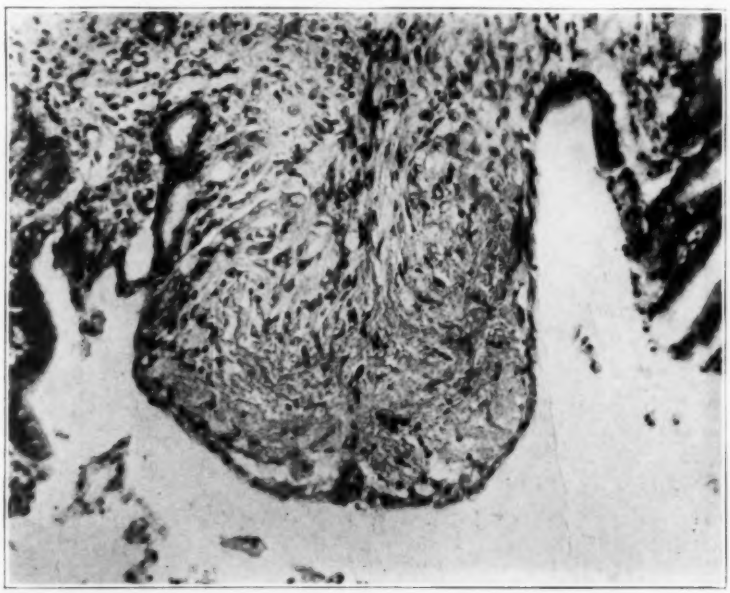


Fig. 3.—Section through edge of ulcer. This illustrates the change in the epithelium of the duodenal mucosa, the granulation tissue entirely covered by epithelium, the participation in the healing process by one of the duodenal glands, and the very active formation connective tissue. (× 120.)

4. Mann, F. C.: The Chemical and Mechanical Factors in Experimentally Produced Peptic Ulcer, Surg. Clin. N. Am. **5**:753-775, 1925; Production and Healing of Peptic Ulcer; An Experimental Study, Minnesota Med. **8**:638-640, 1925.

In the two cases of ulcer previously reported, search was made for bacteria in the tissues to determine whether the ulcers of the newborn were not also due to streptococci. Although several of the usual methods of staining were tried, no bacteria were found in the tissues. Some large rods and large cocci were found on the surface but they were judged to be saprophytes.

While the ulcer reported here was being studied, sections from the other two ulcers, as well as of this one, were stained and examined according to the technic of Rosenow, and in all three specimens diplococci, sometimes cocci in short chains, were found. Large numbers of organisms were demonstrated in the necrotic sloughing tissues (Fig. 4) and smaller numbers of diplococci in the deeper layers of the tissue of the ulcers, mostly adjoining nests of cellular infiltration (Figs. 5 and 6). After long search, several diplococci were demonstrated in

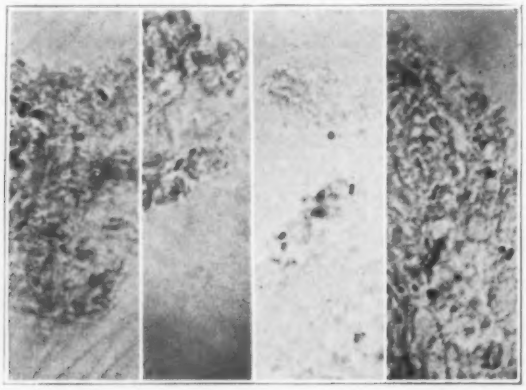


Fig. 6.—Diplococci in tissues of ulcer of the duodenum in Case 2, reported previously.

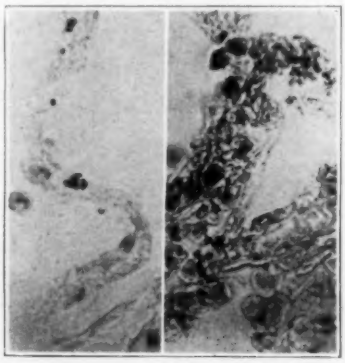
the wall of the thrombosed vessel in the cases reported previously. In the depths of the tissue, only diplococci were found, whereas on the surface a few large bacilli and cocci were also present. Organisms were not demonstrable in the normal tissue remote from the ulcer. The diplococci are morphologically identical in the three cases, and are similar to those found in gastroduodenal ulcers from older persons.

COMMENT

I feel that the facts presented here, considered in connection with the findings of Rosenow, and of Gerdine and Helmholz, add to a body of evidence which already very emphatically shows the importance of infection in the etiology of peptic ulcers occurring in patients of all ages.

speculation, and, as is usual when definite facts are lacking, numerous theories and hypotheses concerning their origin have been formulated. The fact that none of these has been accepted as the explanation of the cause shows that the question of the etiology of duodenal ulcer in the new-born is still an open one.

Evidence which proves that infection plays the major part in the production of gastric and duodenal ulcers has accumulated during the last few years. Notable contributions along this line are those of Rosenow [6] and of Gerdine and Helmholz.[7] The former demonstrated streptococci in the ulcer tissue of specimens removed at operation in a large series of cases. He succeeded in growing these organisms and also found that, on intravenous injection into animals, they tended to localize in the stomach and duodenum, producing lesions resembling early peptic ulcers.



A B

Fig. 5.—Diplococci in the tissue of the ulcer of the duodenum in Case 1, reported previously.

Gerdine and Helmholz, following Rosenow's technic, studied twenty-five duodenal ulcers which occurred in infants beyond the neonatal period of life. Partly because this group of ulcers occurred in a relatively short period of time they were assumed to be infectious in nature. This assumption was borne out when streptococci were demonstrated in nearly all of them.

Thus, an organism has been found in peptic ulcers which will account for their formation in patients, ranging in age from a few weeks to 70 or more years.

---

6. Rosenow, E. C., and Sanford, A. H.: The Bacteriology of Ulcer of the Stomach and Duodenum in Man, J. Infect. Dis. **17**:219-226, 1915. Rosenow, E. C.: The Causation of Gastric and Duodenal Ulcer by Streptococci, J. Infect. Dis. **19**:333-384, 1916.

7. Gerdine, L., and Helmholz, H. F.: Duodenal Ulcer in Infancy and Infectious Disease, Am. J. Dis. Child. **10**:397-409 (Dec.) 1915.

OSTEOMALACIA IN CHILDREN

A STUDY OF THE MINERAL METABOLISM *

HUGH L. DWYER, M.D.
AND
ORREN S. ECKELBERRY, A.B.
KANSAS CITY, MO.

As the name implies, osteomalacia is a disease in which the bones become soft, bend and break easily, resulting oftentimes in extreme deformities. It is extremely rare in children, the condition being preeminently one of early adult life, more frequent in women and usually associated with the puerperium.

Virchow described it as a dissolution of lime salts. He regarded the bone as a finished product or inert substance not undergoing active metabolism, and believed that in osteomalacia the mineral elements were dissolved and the organic matrix left. Cohnheim [1] expounded the modern theory, namely, that bone undergoes active metabolism and while mineral substances were being given up by the bone in osteomalacia; new osteoid tissue replaced it. Many writers contend that the disease is identical with rickets.

The age period in which osteomalacia makes its appearance, and its association with pregnancy, forms a basis for the classification of the various forms of the disease by Locke,[2] as follows:

AGE PERIOD

1. *Puerperal Form.*—This form occurs in women who have had numerous and frequent pregnancies. It rarely begins before the second pregnancy and may improve after delivery, only to recur in worse form in succeeding pregnancies. The demand for calcium becomes great during the last months of pregnancy, calcium being deposited only in the last three months of fetal life, and this entails a drain on the store of calcium in the mother's skeleton.

2. *Nonpuerperal Form.*—In this form the sexes are about equally affected, the course is slow and progressive, and the deformities less severe and more generalized, not affecting the pelvic bones particularly.

3. *Hunger Osteomalacia.*—This is the form most frequently observed during the last few years in Germany. An extremely rare

* Received for publication, Dec. 30, 1925.

* From the Departments of Pediatrics and Biological Chemistry, University of Kansas, and the Children's Mercy Hospital.

1. Cohnheim, J., Quoted by McCrudden: Endocrinology and Metabolism, New York, D. Appleton & Company, 1922.

2. Locke, E. A.: Oxford Medicine, London, Oxford University Press, 1921.

It is unusual to find a duodenal ulcer in a new-born infant who has died with the syndrome known as hemorrhagic disease, a condition apparently present in this case. In other cases observed at the Mayo Clinic, the bleeding and coagulation times were normal, and there was no bleeding from other parts of the body. That the bleeding time was prolonged in this case and that there was bleeding from the umbilicus must be regarded as a coincidence. I have been unable to find any report in the literature of the simultaneous occurrence of these conditions.

The prognosis in cases of melena neonatorum is important. In a number of cases, variously stated at from 25 to 50 per cent., bleeding ceases after a week or ten days, and recovery is complete. The source of bleeding is not known. On the basis of the histologic findings in this case, however, it may be said that nearly complete healing occurred in the same length of time as is required for clinical improvement and cessation of symptoms. It is not unlikely that in many cases recovery is brought about by a similar process of healing of duodenal ulcer.

SUMMARY

Careful search will reveal peptic ulcer in a larger number of cases of melena neonatorum. In three cases studied, streptococci or diplococci were demonstrated in the tissues of the ulcers. It is believed that these must be the chief etiologic agents. Healing of duodenal ulcers begins very early and proceeds rapidly, so that, under proper conditions, the injury may be entirely repaired in a few days, an additional reason why they are so difficult to find. The rapidity of the healing of duodenal ulcer probably accounts for many of the recoveries from melena neonatorum.

History.—The parents were living and well, and the patient was their only child. Her trouble started at the age of 6 months, when she sustained a fracture of the humerus from a slight trauma. Since that time she has suffered from many fractures of the humeri, radii and femora.

Physical Examination.—She was a poorly nourished child with prominent frontal and parietal bosses, and a pronounced "pigeon-breast" deformity. There was a general muscular weakness and she complained of vague pains in her ars and legs. Harrison's groove, epiphyseal enlargements and flaring of the lower border of the thorax, evidence of rachitic deformities, were found. The humerus, femur and tibia on both sides presented deformities. The bilateral

Fig. 1 (Case 1).—Deformity of arms and legs, unable to stand alone.

symmetry of these deformities was noteworthy. With the exception of a functional cardiac murmur the positive findings were confined to the skeleton (Fig. 1).

Roentgenographic Examination.—There was evidence of multiple fractures of the long bones which healed with poor union. Angular deformities at the neck of both femora and humeri, thinning of the cortex, rarefaction of the bone and a symmetrical curving of long bones were found. The epiphyses were widened, and an area of extreme rarefaction was present in the distal end of the right humerus (Fig. 3).

condition before the World War, it assumed great proportions in the postwar period when the food shortage became acute. There is no doubt in the minds of those familiar with the condition as it occurred in Germany that undernutrition was the cause of the disease. Frequently, there were several members of the same family affected, and the disease was especially prevalent in certain sections in which food shortage was greatest. A full normal diet for a few weeks was followed by improvement.

Hutchison and Stapleton,[3] who argue for the importance of lack of sunlight and exercise as a causative factor, more important than dietary deficiency, question the correctness of those who conclude that there is a hunger type of osteomalacia, and mention the fact that the great famines of India were not followed by this malady.

Some of the ardent proponents of endocrine theories go so far as to suggest that the undernutrition, per se, was not the prime factor, but that some vitamin deficiency may have led to a suppression of parathyroid function and this brought about the disease.

4. *Senile Form.*—This form has been recorded in a few instances, and is characterized by its mild, chronic course. The existence of this type of osteomalacia has been doubted by several writers. Some look on this form as manifestations of bone neoplasms and others as osteoporosis. McCrudden regards the process as one of osteoporosis, saying the bones become thin but not soft, because the increased bone catabolism is not followed in the aged by a deposition of new osteoid tissue.

5. *Juvenile Osteomalacia.*—It is with this form that we are chiefly concerned in this report. This variety is quite rare and is usually found in adolescence. There is no evidence that heredity plays a part in its development.

Two children entering the Children's Mercy Hospital presented the clinical features of osteomalacia, and we were afforded an opportunity of making studies of the inorganic metabolism. One of these patients exhibited pain and muscular weakness, giving the impression that the disease was active. The other patient exhibited much greater bony deformity but no weakness or pain; he had been under the care of competent physicians for several years and it is probable that the condition had been influenced by treatment.

REPORT OF CASES

CASE 1.—F. D., a girl, aged 5 years, who weighed 12.3 kg. (27 pounds), was admitted to the orthopedic service of Dr. R. M. Schauffler, on Oct. 23, 1923, because of pain in the limbs, muscular weakness, skeletal deformities and inability to walk.

3. Hutchison, H. S., and Stapleton, Grace: Brit. J. Child. Dis. **21**:96 (April-June) 1924.

ture of right femur" (April 30). "Long spiral fracture of the left humerus at junction of middle and lower third" (June 12). "Oblique fracture of middle and upper third of right humerus—there are several fragments and evidence of pathology within the bone. An old fracture of lower third shows good bony union" (June 28).

After several unsuccessful attempts to correct her deformities, the patient was discharged unimproved. The results of a study of her mineral metabolism are found in Table 1.

Fig. 3 (Case 1).—Fracture and curving of the humerus, with rarefaction of the bone most marked in the epiphyses.

CASE 2.—J. B., a boy, aged 12 years, weighed 20 Kg. (44 pounds), was admitted to the orthopedic service of Dr. C. B. Francisco on July 1, 1923.

Family History.—The father was living and well. The mother had died of pulmonary tuberculosis; she had not been as robust as her brothers and sisters, and was regarded by the family physician as a child "whose bones were not good and easily broken." During her childhood she sustained six fractures.

Laboratory Examination.—The blood calcium was 10.6 mg., and phosphates 5.2 mg. per hundred cubic centimeters. Erythrocytes, 3,200,000; leukocytes, 10,000; hemoglobin, 70. The urine was normal. The Pirquet test was negative. The blood calcium was checked several times and was always found within normal limits.

Clinical Course.—The child remained in the hospital for ten months without any change in her condition. She became ill with bronchopneumonia from which she recovered slowly. Metabolism experiments were carried out imme-

Fig. 2 (Case 1).—Angular deformity of both femora, poor union of old fractures and widening of the epiphyses.

diately after her recovery. She seemed to have considerable pain, presumably from her bones, but never any muscle spasm or tetany that is sometimes found in osteomalacia. Any muscular effort was liable to result in a fracture. A brief résumé of the roentgenographic examinations on her chart is illustrative.

"Pathological fracture of left femur" (November 15). "Long spiral fracture through upper third of right radius" (December 8). "Pathological frac-

The first, of the clavicle, occurred when she was 6 years old. The others were in the femur and tibia of both legs. The left leg was slightly shorter than the right, which necessitated wearing a special heel. Her deformity did not handicap her and was regarded by her to be the result of poor surgery at the correction of one of her first fractures. All of her fractures were brought about by means much more severe than those causing fractures in her son.

Patient's History.—The boy was normal until 18 months of age, when he sustained his first fracture. Since that time he has had one fracture of the

Fig. 4 (Case 1).—Left femur showing fracture, curving and rarefaction.

clavicle and fifteen of the femora. These have resulted from slight muscular efforts, such as turning suddenly while bearing his weight on one leg or even from falling out of bed. Healing takes place slowly and with marked deformity. Below the knees both legs have become flattened laterally and bent backward. There had been no fractures of the tibiae or upper limbs. Muscular development was poor in the lower limbs, but apparently normal in the upper. His fractures occurred from six to twelve months apart.

TABLE 1.—*Intake and Excretion of Calcium, Magnesium and Phosphorus Pentoxide*

Urine	Calcium, Gm.	Magnesium, Gm.	Phosphorus Pentoxide, Gm.
2/19/25	0.065	0.087	0.981
2/20/25	0.072	0.057	0.996
2/21/25	0.086	0.074	0.625
2/22/25	0.096	0.079	0.616
2/23/25	0.055	0.092	0.967
2/24/25	0.073	0.070	0.813
2/25/25	0.140	0.103	0.670
2/26/25	0.077	0.043	0.642
2/27/25	0.094	0.055	0.836
Total	0.758	0.660	7.146
Feces			
3 days	1.905	0.826	1.005
3 days	1.625	0.513	1.473
3 days	2.120	0.673	1.083
Total	5.650	2.012	3.561
Excretion	6.408	2.672	10.707
Intake	6.094	3.031	12,374
Balance	−0.314	+0.359	+1.667

TABLE 2.—*Intake and Excretion of Calcium Monoxide, Magnesium and Phosphorus Pentoxide*

Urine	Calcium Monoxide, Gm.	Magnesium, Gm.	Phosphorus Pentoxide, Gm.
2/19/25	0.044	0.069	0.696
2/20/25	0.015	0.148	0.611
2/21/25	0.093	0.065	0.717
2/22/25	0.071	0.132	0.663
2/23/25	0.043	0.145	0.637
2/24/25	0.028	0.073	0.608
2/25/25	0.089	0.101	0.644
2/26/25	0.080	0.147	0.600
2/27/25	0.067	0.089	0.676
Total	0.530	0.970	5.852
Feces			
3 days	2.590	0.593	2.120
3 days	2.812	0.650	1.675
3 days	2.790	0.702	1.325
Total	8.192	1.945	5.120
Excretion	8.722	2.915	10.972
Intake	9.923	3.496	12.128
Balance	+1.201	+0.581	+1.156

defective nutrition. This boy was a contented patient who did not complain; he sustained two or three fractures during his first year in the hospital, one resulting from falling out of bed.

The legs were so twisted that amputation above the knee was considered by the orthopedic surgeons, with a view of placing him on a wheeled platform to move about. However, it was decided that attempts at straightening the limbs by osteotomy would be made. The results were quite successful, so that

Fig. 6 (Case 2).—Pronounced outward bowing of the right femur, several old fracture sites and rarefaction.

a little weight could be borne on the feet, and with the use of crutches he got about fairly well after having spent all his life in bed or in a wheel chair.

The bone at operation was easily cut with a heavy knife, and the operator described it as "the consistency of hard rubber." A piece of this bone was examined by Dr. H. R. Wahl, whose report follows:

"Gross Pathology: Material consists of a piece of cortical bone with a small amount of medullary tissue on one side. The piece measures 15 by 6 by

Physical Examination.—The frontal and parietal bosses were prominent, presenting a flat, square head. There were severe grotesque deformities of the lower limbs. Both femora were bent outward at nearly right angles in the upper third. The thighs appeared very short due to this angulation. Both tibiae were curved backward at the middle of the shaft, and were flattened laterally to almost a blade-like deformity (Fig. 5).

Roentgenographic Examination.—The skull showed slight thickening of both inner and outer tables. The sella appeared to be normal. The bones of the upper limbs showed no evidence of pathology. The femora showed marked bowing laterally, with evidence of softening in the medullary canal. There

Fig. 5 (Case 2).—Severe twisting deformities of the legs. The arms are not involved. The tibiae flattened to a blade-like deformity.

was anterior bowing of the tibiae and fibulae, with the same changes as in the femur. The vertebrae showed normal development, with normal textural outlines, no abnormal softening or productive bone changes.

Laboratory Examination.—Erythrocytes, 3,700,000; leukocytes, 6,000. Blood calcium 10.5 mg. and phosphates 4.8 mg. per hundred cubic centimeters. The urine was normal.

Clinical Course.—There was no muscular pain or weakness. The neuromuscular system and mentality were found to be normal. The teeth showed

METABOLISM STUDY

The patients were given a diet somewhat restricted to facilitate analysis, but well balanced and of sufficient caloric requirements. The children were attended constantly, and no known error resulted in the collection of urine and feces and in measuring the intake. The diet was started three days before beginning the experiment. The stools

Fig. 8 (Case 2).—The right tibia and fibula after surgical correction. The fibula shows little contrast from the soft parts and the cortex of the tibia is extremely thin.

were marked and collected in three-day periods. These three-day lots were mixed, dried, weighed and run in duplicate. The urine was collected in twenty-four-hour specimens and was analyzed daily. Creatinin determinations were made to check the accuracy of urine collection.

5 mm. The cortical portion is somewhat roughened and chipped off in places, and the medullary is porous and friable in character. No exudate is noted.

"Histologic Pathology: There are rather thick, heavy and irregular bands of osteid tissue containing large numbers of bone corpuscles. These corpuscles do not stand out quite distinctly. The tissue does not stain very well. The marrow substance is rather indistinct, rather scanty and seems to be somewhat disintegrated. The general architecture is rather irregular, coarse and heavy.

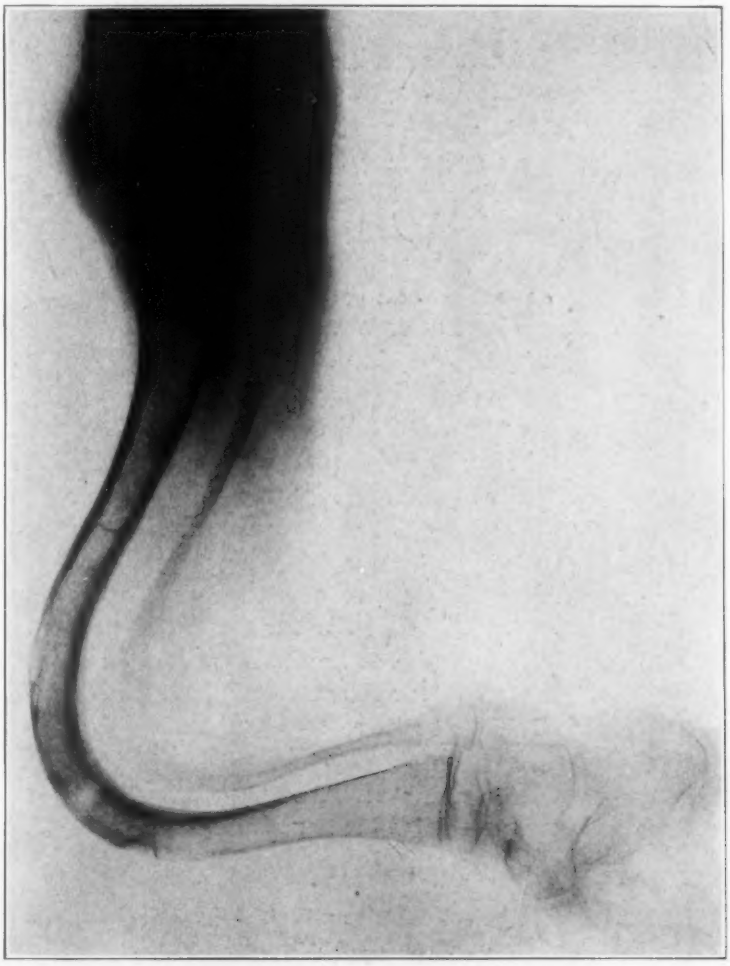
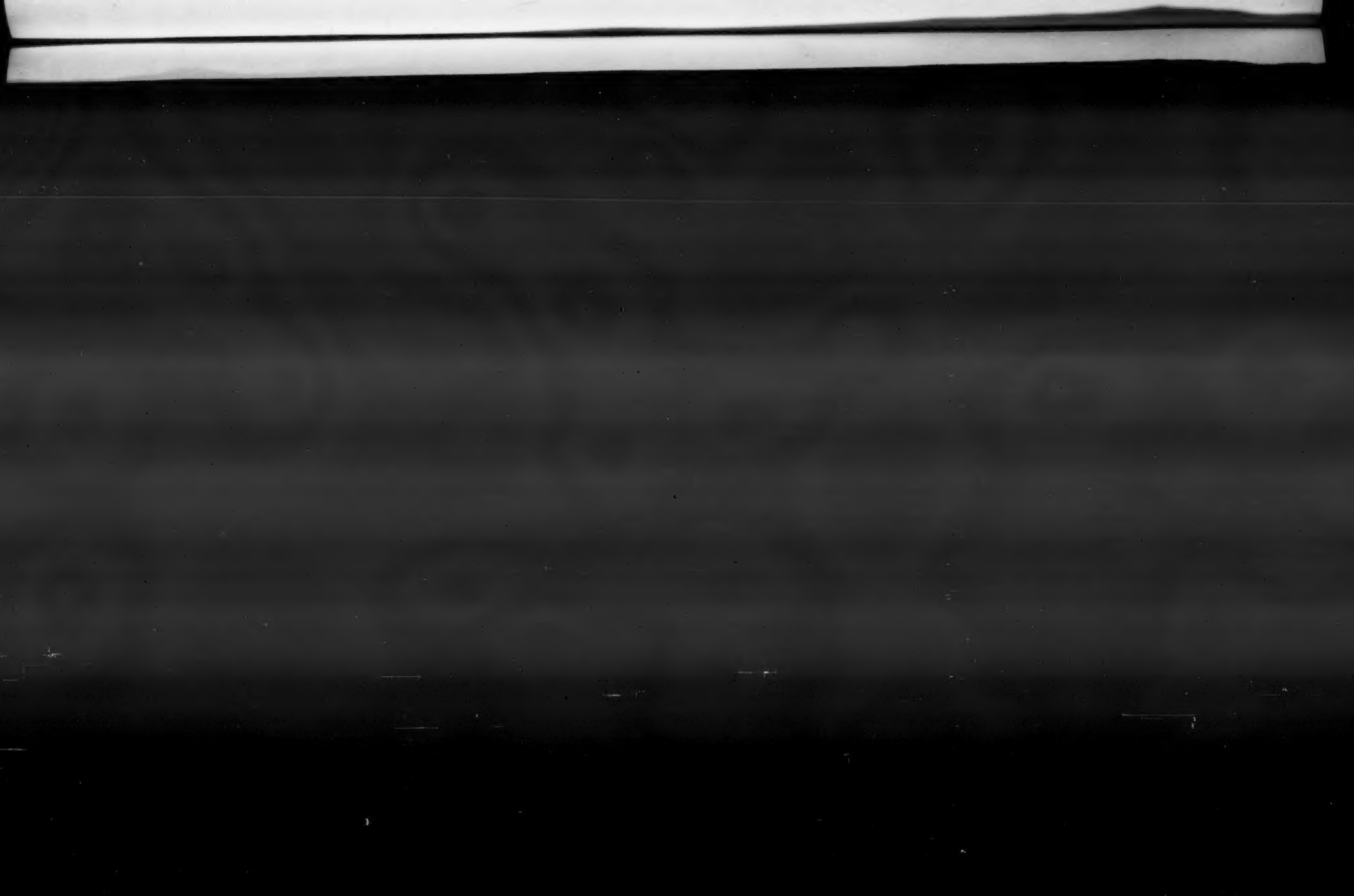


Fig. 7 (Case 2).—Rarefaction and extreme deformity of the left tibia and fibula.

"In one of the sections, the marrow substance was much more abundant and showed considerable congestion and in places some hemorrhage. In some places there seemed to be beginning tendency to calcification and irregular and incomplete ossification. In a few foci, the bone trabeculae seem to be undergoing a disintegration, leaving a sort of crumbling detritus.

"Diagnosis: Osteoid bone; osteomalacia."



The calcium and magnesium were determined by McCrudden's method,[4] and the phosphorus by the Bell-Doisy method as modified by Briggs.[5]

F. D. (Case 1, Table 1) shows a calcium loss of 5.15 per cent, and retention of 11.8 per cent magnesium and 13.47 per cent phosphorus. Clinically, she apeared to be more active than the boy, although her deformities were not so pronounced. She was quite weak and her limbs were painful.

J. B. (Case 2, Table 2) shows a retention of all elements, 12.1 per cent calcium, 16.62 per cent magnesium and 9.53 per cent phosphorus.

These figures indicate a definite reduction of all mineral elements, sufficient to reach a negative balance in calcium of one patient. In a normal child, McCrudden and Fales[6] found a retention of 17 per cent calcium, 22 per cent magnesium and 25 per cent phosphorus.

Working with normal infants on cows' milk mixtures, Daniels and Stearns[7] found from 26 to 35 per cent calcium retained and 27 to 37 per cent of the phosphorus. In two normal infants, Shohl and Sato[8] found a calcium retention of 24 to 27 per cent, phosphorus 17 and 18 per cent and magnesium 37 per cent. One of their infants had a magnesium loss of 3 per cent.

A loss of 24 per cent calcium in a patient with osteomalacia was reported by Goldthwait, Painter, Osgood and McCrudden.[9] Limbeck[10] reported a loss of 89 per cent.

Miles and Feng[11] found a negative calcium balance in three of their four osteomalacia patients. All had a positive phosphorus balance. These were adult females, in three of whom the symptoms began in the puerperium. After the addition of cod liver oil alone, and in combination with either calcium lactate or calcium phosphate, they were able to bring about marked retention. In one patient receiving olive oil with calcium lactate, the calcium balance remained negative.

In cases of active rickets, Telfer[12] found the calcium excretion reduced to the point of balancing the intake, but not reaching a negative balance.

---

4. McCrudden, F. S.: J. Biol. Chem. **7**:83, 1909-1910; ibid. **10**:187, 1911-1912.
5. Briggs, A. P.: J. Biol. Chem. **53**:13 (July) 1922.
6. McCrudden, F. S., and Fales, Helen: J. Exper. Med. **15**:450, 1912.
7. Daniels, A. L., and Stearns, G.: Nitrogen and Mineral Balances in Infants Receiving Cow's and Goat's Milk, Am. J. Dis. Child. **30**:359 (Sept.) 1925.
8. Shohl, A. T., and Sato, A.: J. Biol. Chem. **58**:257 (Nov.) 1923.
9. Goldthwait, J. E.; Painter, C. F.; Osgood, R. B., and McCrudden, F.: Am. J. Physiol. **14**:389, 1905.
10. Limbeck: Quoted by McCrudden, Footnote 1.
11. Miles, L. M., and Feng, Chih Tong: J. Exper. Med. **41**:137 (Jan.) 1925.
12. Telfer, S. V.: Quart. J. Med. **16**:63 (Oct.) 1922.

ETIOLOGY

Because of the frequent occurrence of osteomalacia in the puerperium, many theories of endocrine imbalance have been entertained.

The old theories of infection and of acid dissolution of the bones, find no support in the work of recent years. Virchow believed that a hyperemia of the bone resulted in the acids of the blood dissolving the earthy salts. This process at that time was thought to be one of simple halisteresis. McCrudden has shown the fallacy of these views in his work on bone analysis, showing that magnesium phosphate is increased in the bone of osteomalacia, and this being a more soluble salt than calcium. Recent workers in hunger osteomalacia have found a lowered carbon dioxid tension in the alveolar air, and believe that this enables the blood to take up lime salts from the bone. The serum calcium, however, has not been found high except in the cases reported by Scott.[13]

Of the internal secretions, that of the ovary has received most attention. Removal of the ovaries and also removal of the uterus were found to bring about the amelioration of the condition. McCrudden has reviewed the reports of these cures and finds that many were of temporary benefit only; he believes that the prevention of further pregnancies was the only factor in those showing improvement. Not much evidence of thyroid disturbance has been advanced as a cause. The bone changes following extirpation of the parathyroid have been compared to those in osteomalacia. Likewise, removal of the suprarenals in goats was followed by similar bone changes, and the therapeutic use of epinephrin has been advocated by Bossi and Edelman.

Dalyell and Chick,[14] working with hunger osteomalacia in Vienna, experimented on the therapeutic effects of various fats, and concluded that the vitamin fat soluble (A) was the curative factor, cod liver oil giving the best results. Hume and Nirenstein,[15] when plant oil failed, brought about cures in these patients with cod liver oil.

In India, the disease seems to be quite prevalent. Scott investigated eighty-one cases; one-third of these were Mohammendans living under the purdah custom. The remaining subjects were Hindus who do not practice strict purdah. These were all in females. These women spend their lives in seclusion, seldom leaving their homes. Early marriage and prolonged lactation were practiced, the average age of marriage being 13.2 years and the average nursing period being 2.4 years. All of these were possible etiologic factors. Observing the same type of cases, Hutchison and his associates regard the lack of exercise of prime

13. Scott, A. C.: Indian J. M. Res. **4**:140 and 169 (July) 1916.
14. Dalyell, E. J., and Chick, H.: Lancet **2**:842 (Oct. 22) 1921.
15. Hume, E. M., and Nirenstein, E.: Lancet **2**:849 (Oct. 22) 1921.

importance, and the lack of sunlight secondary. This is essentially the view of the Glasgow school in regard to the etiology of rickets.

Almost from the time the disease was first recognized, there has been considerable discussion concerning its identity with rickets. Histologic studies in the early days were offered as evidence of the similarity of the two conditions, and today students of metabolism, principally the English workers, offer metabolic and roentgenographic evidence that the two diseases are identical. But there are many competent observers who contend for a separation of the two conditions. It would seem from the few cases observed in this country that the disease has certain clinical features, at least, that distinguish it from rickets.

Cohnheim believed there was a difference between rickets and osteomalacia. He described the process in rickets as one in which osteoid tissue, a soft organic substance that normally forms the framework of bone, but without the bone-earth that should be combined with it, is found at the junction of the epiphysis and diaphysis, as well as beneath the periosteum. The process in osteomalacia, he asserted, was a substitution of osteoid tissue for true bone tissue and the areas involved were not at the epiphyseal ends or immediately beneath the periosteum, but in the interior of the fully formed bone in close proximity to the Haversian canals. This, we believe, is the accepted view at the present time. In short, rickets is a faulty deposition of mineral matter in young bone in areas that have not yet undergone ossification, and osteomalacia is a substitution of organic matter for mineral matter in mature bone.

If this explanation is correct, it follows that osteomalacia and rickets differ in two important features, namely, the part of the bone involved and the age incidence. Metabolism studies show that the two conditions are alike, differing only in severity.

Hutchison and Stapleton,[16] in a lengthy review of the existing differentiation of early rickets, late rickets and osteomalacia, state that there is no justification for the separation, that the conditions are identical and represent rickets at different ages. Stapleton[17] later analyzed seventy-three cases of late rickets and osteomalacia occurring in Delhi. She states that "osteomalacia was diagnosed when there was pain in the lumbosacral region, of the spine and thighs, tenderness of the bones, difficulty in rising and walking and a waddling gait." She believes that there is no sharp distinction clinically between late rickets and osteomalacia, and finds intermediate stages showing characteristics of both. The difference in the symptoms appear to be due to conditions on the tissue depending on the age of the patient.

---

16. Hutchison, H. S., and Stapleton, Grace: Brit. J. Child. Dis. **21**:96 (April-June) 1924.
17. Stapleton, Grace: Lancet **1**:1119 (May 30) 1925.

American observers, however, do not see the type of rickets known as "late rickets," or at least do not differentiate it from osteomalacia. Of late rickets, Holt and Howland [18] in 1916, wrote, "It is very rare in this country. We have never seen a case." Griffith [19] says "the condition is rare, the final deformity very decided, and the instances of late rickets are properly classified as osteomalacia." We are inclined to look on rickets as a self-limited disease, the active stage not extending beyond the second year of life, and the bony changes (unless very pronounced) largely disappearing in childhood. According to the British writers, early rickets is regarded as an "incomplete calcification and ossification of the bone commencing during the first four years of life, late rickets a similar process setting in for the first time after four years of age, and osteomalacia as a decalcification of the bones after the cessation of the period of growth, that is, after 18 to 20 years of age."

In our two patients there is no evidence of endocrine disturbance, and no reason to believe that dietary deficiency is responsible for the condition. The use of cod liver oil and a proper diet did not stop the progress, apparently, in one of our patients. In the other, the disease appeared to be stationary, although fractures occur frequently, probably because the architecture of the bone had been changed by repeated faulty union of older fractures. The influence of lack of exercise is difficult to estimate. The disease started early in both children, and they have spent practically all their time in bed. It would seem that as the condition began in infancy, lack of exercise could hardly be looked on as an important etiologic factor. It seems unlikely that lack of sunlight and fresh air are causative factors in these children. Both of our patients show rachitic changes, especially of the thorax and bosses. It would hardly be expected that they could escape rickets, owing to their poor nutritional state, and a life of confinement, due to their physical condition.

The history of repeated fractures in the mother of one patient (J. B.) is unusual. It is unlikely that she would have had six fractures unless there was some bone pathologic changes. We have found no case in the literature in which heredity was a factor.

SUMMARY

Two cases of osteomalacia occurring in children are reported. Studies on the mineral metabolism indicate that there is a lowered retention of calcium, magnesium and phosphorus. In one patient the calcium loss reached a negative balance. A brief review of the literature on the etiology of osteomalacia and its relation to rickets is presented.

18. Holt, L. E., and Howland, J.: Diseases of Infancy and Childhood, New York, D. Appleton & Co., 1916.

19. Griffith, J. P. C.: Diseases of Infants and Children, Philadelphia, W. B. Saunders Company, 1919.

CHYLOTHORAX IN THE NEW-BORN INFANT

REPORT OF A CASE *

CHESTER A. STEWART, M.D.
AND
H. P. LINNER, M.D.
MINNEAPOLIS

Recently, a most unusual and at first perplexing intrathoracic condition was discovered in a new-born infant, which we considered of sufficient rarity and interest to justify reporting.

REPORT OF CASE

B., a boy, was born Oct. 2, 1924, weighing 3,250 Gm. The delivery was entirely normal and respiration started promptly and the baby appeared to be perfectly well until the fourth day after birth. At this time he suddenly became quite cyanotic and had great difficulty with respiration. One grain of caffein sodium benzoate was administered by hypodermic injection and oxygen inhalations were given, following which the condition of the baby distinctly improved. In addition, 30 cc. of citrated blood was injected subcutaneously. A short time later, an examination of the baby revealed that the right side of the thorax failed to expand on inspiration. The percussion note was dull over the entire right side of the chest, and the breath sounds in this area were barely audible. No râles were heard. A diagnosis of hydrothorax was made, the etiology of which was perplexing, particularly since the baby had a normal rectal temperature (98.6 F.) and also since the onset of symptoms had occurred very suddenly. A roentgenogram of the chest was taken, which revealed an extensive accumulation of fluid in the right pleural sac. The chest was aspirated, and 110 cc. of fluid was removed, which resembled egg yolk in color. On examination, the aspirated fluid was found to be entirely devoid of cells, leukocytes and bacteria, and proved to be sterile on culture. Following the removal of this fluid, the difficulty in respiration disappeared for a few hours. The following day, however, a recurrence of respiratory embarrassment necessitated aspiration again, and 150 cc. of yellowish fluid was removed, which microscopically resembled that removed the day previous. The fluid was stained with sudan III, and was found to contain innumerable fat droplets taking a bright red stain. In addition, a test for bile was negative. It now became evident that we were dealing with a case of chylothorax, due possibly to rupture of the thoracic duct. The golden yellow color of the chylous fluid apparently was derived from the pigment (lactochrome) present in the colostrum the baby obtained at the breast, although no attempt was made to identify this pigment aside from excluding the presence of bile in the intrathoracic fluid.

The chest was aspirated the third time on October 11, and daily thereafter until October 22, on which date the baby died, weighing 2,955 Gm. On October 11, nine days after birth, the aspirated fluid was distinctly less yellow than on previous dates, and became milky white the following day. At this time, when the baby was 10 days of age, 3 minims of sudan III were given with each feeding. The following five days 0.5, 1, 2, 2.5 and 3 cc. respectively, of this dye

---

* Received for publication, Feb. 24, 1926.

* From the Department of Pediatrics, University of Minnesota.

* From a series of necropsies conducted for the children's bureau in the Pathology Laboratory, under the supervision of Dr. F. L. Adair.

were given with the feedings, but at no time were we able to stain the fat droplets in the chylous fluid by the oral administration of this amount of sudan III. On October 15 (thirteenth day of life) one and one-half grain of sterile congo red was injected intraperitoneally, and two days later the fluid aspirated from the chest had acquired a salmon pink color. That this color was due to the presence of congo red was proved by chemical tests (addition of hydrochloric acid). Four days later the fluid became milk white again, and the presence of congo red could no longer be demonstrated. During the sixteen days of life following the onset of symptoms, a total of 1,155 cc. of fluid had been removed from the right thoracic cavity. An endeavor was made each time to remove only sufficient fluid to relieve the respiratory embarrassment, with the hope that leaving some fluid in the pleural sac would raise the pressure sufficiently in this space to prevent mechanically continued leakage from the thoracic duct. The possibility of surgical intervention was considered, but was abandoned.

Extensive hydrothorax on right side, with displacement of mediastinum to the left.

Necropsy.—At necropsy, aside from the general emaciation, the pathologic findings were confined entirely to the thorax. The posterior mediastinum was displaced toward the left. The right pleural sac was completely filled by a milky white fluid, which caused a general atelectasis of the right lung. After the complete removal of this fluid on exerting pressure on the stomach and other abdominal viscera, it was possible to detect a slight seepage of chylous fluid from a point in the posterior mediastinum adjacent to its attachment to the diaphragm. An unsuccessful attempt was made to dissect the thoracic duct; thus it was necessary to assume that the chylous fluid present in the pleural sac came either from the duct or from some large tributary to the duct, more probably from the former.

A survey of the literature reveals the fact that very few cases of chylothorax in young infants have been reported. Baldwin [1] collected forty-seven genuine and fifteen doubtful cases of chylothorax from the literature, the youngest being a patient aged 2 years. We have been able to find records of a total of three cases reported since 1902 in infants less than 1 year of age. Muttermilch [2] saw an infant, aged 5 months, develop chylothorax subsequent to falling from bed. This infant apparently recovered. Jennings [3] saw the condition in an infant, aged 9 months. The youngest infant having chylothorax reported to date probably is that of Pisek.[4] At the age of 9 weeks this baby became ill, and in a few hours had difficult and rapid breathing accompanied by convulsions. In the course of five days, 9 ounces of milky fluid were removed from the right thoracic cavity. The baby was given 7.5 Gm. of sudan III by mouth, following which the intrathoracic fluid acquired a pink stain. This infant apparently recovered.

COMMENT

The case of chylothorax reported in this paper apparently occurred in the youngest infant recorded to date. Among the observations of particular interest in connection with this case was the presence of a deep yellow color of the chylous fluid during the first few days of life due to some pigment other than bile, most probably lactochrome derived from colostrum the baby obtained from the breast. This finding suggests that the pigment present in colostrum (lactochrome) is absorbed into the lymphatics from the intestinal tract, and enters the general circulation of the infant during the first few days of life. It is possible, therefore, that some cases of so-called icterus neonatorum may be due in part at least to carotinemia, the pigment being derived from the colostrum. The possibility of icterus neonatorum resulting from carotinemia is reserved for a future publication.

SUMMARY

A fatal case of chylothorax in an infant, aged 4 days, due apparently to a rupture of the thoracic duct is reported.

In the amounts given, the oral administration of sudan III failed to stain the fat droplets in the chylous fluid.

The golden yellow color of the chylous fluid present the first few days apparently was due to lactochrome (carotin, largely) derived from the colostrum the baby obtained at the breast.

Following the injection of sterile congo red into the peritoneal cavity, the dye appeared in the chylous fluid in the pleural sac.

---

1. Baldwin, F. A.: Appendix to Reference Handbook of Medical Science, 1908, p. 463.
2. Muttermilch: Ztschr. f. Klin. Med. **46**:122, 1902.
3. Jennings, C. G., and Rich, H. M.: Arch. Pediat. **25**:195, 1908.
4. Pisek, G. R.: Arch. Pediat. **34**:929, 1917.

RECURRENT VOMITING*

HUGH JOSEPHS, M.D.
BALTIMORE

ETIOLOGY

During the last thirty years, investigators have, at one period or another, announced the discovery of the cause of recurrent vomiting—uric acid diathesis, autointoxication, gastric neurosis, hysteria, chronic appendicitis, postural defect, eyestrain—to name a partial list; yet the real cause is still undiscovered. What is meant by recurrent vomiting? If one should attempt to define it, the definition becomes a description of the disease; if one should attempt to diagnose it, the diagnosis must exclude all other causes of recurring attacks of vomiting. Scarcely ever can one say after a single examination, "This is recurrent vomiting, and nothing else." Yet the picture of the disease with its constantly repeated attacks is a definite one.

In 1901, Marfan[1] described a series of cases, in which there were recurring attacks of vomiting with the early appearance of acetone bodies in the urine and expired air. These cases were identified with similar cases described in this country under the name recurrent vomiting, or cyclic vomiting, so that the finding of acetone bodies in breath or urine has come to occupy a position of importance in the diagnosis. Unfortunately, few patients are seen sufficiently early in the attack to allow the finding of acetone bodies to be of great significance. Moreover, febrile illnesses in children are often accompanied by an early excretion of acetone bodies, and under such conditions it is hard to say whether one is dealing with an attack of recurrent vomiting which has been initiated by an acute infection, or merely with the onset of an acute infection accompanied, as is so often the case, by vomiting.

In 1914, Hilliger[2] studied a child who was subject to recurrent vomiting. He was able to reproduce the attacks by limitation of carbohydrate. The blood sugar concentration was determined during one of these artificial attacks, and it was found to be considerably reduced after twenty-four hours, while that of a normal child remained constant. In 1921, Knoepfelmacher[3] repeated Hilliger's experiments on two patients with recurrent vomiting. He confirmed the observation that

* Received for publication, Jan. 8, 1926.

* From the Harriet Lane Home for Invalid Children, and the Department of Pediatrics of the Johns Hopkins University.

1. Marfan: Arch. de méd d. enf. **4**:641, 1901.
2. Hilliger: Jahrb. f. Kinderh. **80**:1, 1914.
3. Knoepfelmacher, W.: Monatschr. f. Kinderh. **21**:241 (June) 1921.

limitation of carbohydrate would cause an attack of vomiting. He also found a considerable reduction in blood sugar concentration during one of the attacks, but a control determination in a normal child showed almost the same reduction of blood sugar concentration during the same period of time. Ross and I [4] again confirmed Hilliger's observations, especially as regards the blood sugar in a similar case reported a year ago. The study of this case formed the starting point for the present investigation, which is an attempt to throw light on the etiology of recurrent vomiting, as well as to provide a relatively simple laboratory test for the condition.

HYPOGLYCEMIA

In establishing the hypoglycemic nature of recurrent vomiting, I shall first give the more or less direct evidence, that is, the figures obtained during attacks. Of the cases included here, a number have been reported elsewhere in a recent paper.[5] It has seemed best, however, to mention them again for the sake of completeness.

TABLE 1.—*Hypoglycemic Findings in Five Cases*

Name	Age, Years	Color	Blood Sugar During Attack	Time After Onset of Attack	Hours After Last Meal	Acetone	Fever	Normal* Blood Sugar	Remarks
N. H.	2	White	0.058	4 hours	12	+	0	0.100	Two attacks of vomiting, one of convulsions without vomiting; rapid recovery after glucose
R. H.	2	White	0.060	3 days	..	+	0	0.096	Convulsions and vomiting; spontaneous recovery
L. S.	2½	Negro	0.037	1 hour	14	+	+	0.102	Convulsions and vomiting; rapid recovery after giving glucose
S. E.	7	White	0.065	18 hours	24	+	+	0.105	Convulsions and vomiting
	8		0.077	2 hours	12	+	0	0.110	Vomiting only; rapid recovery after glucose
S. S.	7	White	0.060	3 days	..	+	0	.....	Vomiting only
	8		0.072	3 days	..	+	0	0.110	Vomiting only
	9		0.061	3 days	..	+	0	.....	Vomiting only; spontaneous recovery

* Value obtained four hours after a meal following recovery from the attack.

The figures are contained in table 1. A word or two of explanation is necessary. These studies are confined to children who have been admitted to the hospital, and the child who is subject to recurring vomiting attacks of not more than the ordinary severity is generally not brought to the hospital during an attack. It is practically only when such complications as convulsions or acidosis are present that I have been able to study the condition in its active stage. This statement will serve to explain the large percentage of cases with convulsions, as well

4. Ross, S. G., and Josephs, Hugh: Am. J. Dis. Child. **28**:447 (Oct.) 1924.
5. Josephs, Hugh: Fasting as a Cause of Convulsions, Am. J. Dis. Child. **31**:169 (Feb.) 1926.

as the relatively small number of observations. Since two of the children fasted for three days during the attack before a blood sugar determination was made, I ought to include, by way of control, figures from normal children who underwent a fast of this length of time. Such figures from control patients, five in number, may be found in the paper by Ross and myself on the metabolism of L. S., already alluded to.[4] I shall merely state here that none of these five children had a blood sugar concentration of less than 0.070 per cent at any time during a fast of two weeks. I have, therefore, for purposes of diagnosis, considered a blood sugar concentration of less than 0.070 per cent as abnormally low.

These five observations establish beyond question the fact that in some attacks of recurrent vomiting the blood sugar concentration is reduced to a greater extent than during a fast of the same length of time, but that is all they establish. I cannot say from my figures so far that all the attacks in these children are associated with hypoglycemia. Two children have been observed in more than one attack, as the table shows. The figures will be discussed later. On the other hand, from data not included here, I can definitely say that a considerable degree of hypoglycemia can exist without the occurrence of any symptom suggestive of recurrent vomiting, except for drowsiness and the appearance of acetone bodies in the breath and urine.

FASTING

It may be noted that in two of the cases the blood sugar concentration was considerably reduced after a fast of not more than sixteen to eighteen hours, and in a third after a fast of about twenty-four hours. This rapid and excessive fall in blood sugar concentration at the onset of an attack suggested that, in children who were subject to recurrent vomiting, a short fast carried out in an interval between attacks might result in a greater reduction in blood sugar concentration than in normal children.

This fast can be most easily accomplished between supper and breakfast. This is a normal fasting period, and little discomfort is caused by delaying breakfast and keeping the child in bed until 10 o'clock in the morning. The procedure in this investigation was essentially as follows: The child was given a light supper at 5 p. m. Blood was obtained at 9 p. m. The next morning breakfast was delayed, and the child was kept in bed until after 10 a. m., when the second sample of blood was obtained. At the same time a liter of expired air was collected, to be bubbled immediately through Scott-Wilson reagent for determination of the acetone bodies. So far as could be ascertained, the children used for control were normal. Those who had fever or

who were more than 15 per cent underweight were not considered normal for this purpose. In the case of those subject to recurrent vomiting, the test was carried on at a time when the child was not suffering from any infection, and at least a week after recovery from an attack, except in one or two instances in which the child had to leave the hospital before the expiration of a week. The blood samples for sugar determination were taken from the finger capillaries. In procuring them the prick was made deep enough to obtain a spontaneous flow. Blood obtained in this manner should have the same sugar content as arterial blood. In some instances, another sample was taken from an arm vein

TABLE 2.—*Results in Normal Children*

Name	Age	Color	Blood Sugar (Finger Capillaries) 4 Hrs.	Blood Sugar (Finger Capillaries) 16 Hrs.	Inorganic Phosphorus 4 Hrs.	Inorganic Phosphorus 16 Hrs.	Acetone Bodies	Diagnosis and Remarks
W. R.	1 yr.	Negro	0.088	0.085	—	—	0	Normal
	18 mo.	Negro	0.098	0.101	—	—	0	Normal
J. M.	17 mo.	Negro	0.089	0.093	—	—	0	Normal
M. F.	2 yr.	Negro	0.091	0.091	—	—	0	Normal
N.	2 yr.	White	0.098	0.086	—	—	0	Two weeks after operation
C. J.	2 yr.	Negro	0.092	0.091	4.3	3.7	0	Convalescent from pneumonia
M. F.	2 yr.	White	0.096	0.085	—	—	0	Convalescent from burn
M. C.	3 yr.	Negro	0.096	0.098	—	—	0	Normal
J. G.	3 yr.	Negro	0.091	0.082	5.1	4.5	0	Convalescent from pneumonia
D. N.	3 yr.	White	0.095	0.081	—	—	Tr.	Convalescent from a burn
D. T.	4 yr.	White	0.111	0.111	—	—	0	Epilepsy
S. S.	4 yr.	White	0.099	0.094	4.8	4.0	Tr.	Convalescent from dysentery
A. B.	5 yr.	Negro	0.112	0.101	4.3	4.1	0	Tuberculosis (afebrile)
J. McD.	5 yr.	White	0.116	0.106	—	—	0	Epilepsy
E. T.	5 yr.	Negro	0.099	0.096	—	—	0	Normal
L. J.	5 yr.	Negro	0.101	0.101	—	—	0	Normal
V.	5 yr.	White	0.103	0.095	—	—	Tr.	Normal
A. S.	5 yr.	Negro	0.099	0.100	4.4	4.3	0	Convalescent from empyema (5 weeks)
J. D.	6 yr.	White	0.110	0.110	—	—	0	Normal
H. C.	6 yr.	White	—	0.116	—	—	0	Normal
J. J.	6 yr.	Negro	0.103	0.098	—	—	0	Normal
W. B.	7 yr.	White	0.103	0.102	3.8	3.3	0	Convalescent from rheumatic fever
A. J.	8 yr.	White	0.112	0.110	—	—	0	Normal
C. Z.	8 yr.	White	—	0.112	—	—	0	Normal
R. V.	9 yr.	White	0.101	0.094	—	—	0	Normal
A. L.	9 yr.	White	—	0.106	—	—	0	Normal
M. W.	12 yr.	Negro	0.107	0.098	—	—	0	Epileptic
M. C.	12 yr.	White	0.120	0.120	—	—	0	Epilepsy
W. W.	12 yr.	White	—	0.110	—	—	0	Normal

for the estimation of inorganic phosphorus. The sugar was determined by the Fitz modification of the Bang method. Inorganic phosphorus in the serum was determined by the Briggs modification of the Bell-Doisy method.

RESULTS

The results in the case of normal children are contained in table 2. As can be seen from the table, the younger the child the lower is the blood sugar likely to be, but, on the other hand, age has apparently no influence on the rate at which the blood sugar concentration falls during the sixteen to eighteen hours of the fast. It may be readily seen that the sugar concentration of the blood is not reduced to any considerable

extent. The maximum difference between the two values at any time did not exceed 12 mg. per hundred cubic centimeters. The inorganic phosphorus fell to a slight extent. The number of determinations is hardly sufficient to allow any definite conclusions to be drawn in regard to the normal limits for the reduction of inorganic phosphorus.

TABLE 3.—*Results in Children Who Were Subject to Recurrent Vomiting*

Name	Age	Color	Percentage of Blood Sugar (Finger Capillaries) 4 Hrs.	Percentage of Blood Sugar (Finger Capillaries) 16 Hrs.	Inorganic Phosphorus 4 Hrs.	Inorganic Phosphorus 16 Hrs.	Acetone Bodies, 16 Hrs.	Remarks
L. S.	2½ yr.	Negro	0.100	0.076	—	—	+	History of recurring attacks of vomiting with convulsions. Previously reported
S. J. D.	18 mo.	White	0.110	0.081	—	—	Not done	Following an attack of convulsions with coma, cured very rapidly by glucose. No vomiting. Test done three days after recovery
R. H.	2 yr.	White	0.096	0.079	4.2	3.3	+	First attack. Vomiting three days with marked drowsiness and convulsions on third day. Test done two days after recovery. Previously reported
G. M.	2 yr.	White	0.103	0.073	5.2	4.0	Tr.	History of recurrent attacks of convulsions; occasional vomiting. Not observed in an attack. Previously reported
W. A.	2½ yr.	Negro	0.105	0.070	—	—	+	First attack. Vomiting and convulsions with early excretion of acetone bodies. Test done one week after recovery. Previously reported
B. G.	4 yr.	White	0.092	0.074	—	—	Tr.	First attack. Vomiting three days with drowsiness and some acidosis. Test done one week after recovery
S. E.	7 yr.	White	0.110	0.077	—	—	+	History of recurrent attacks of vomiting, two of them accompanied by convulsions. Previously reported
C. H.	7 yr.	White	0.094	0.071	4.6	3.3	++	History of recurrent vomiting with delirium and headache. Not observed in an attack
A. U.	8 yr.	White	0.110	0.086	—	—	+	Subsequent operation followed by vomiting, hypoglycemia, and excessive output of acetone bodies
A. W.	8 yr.	White	0.111	0.061	—	—	Tr.	Preceding operation attended by an attack of vomiting lasting four days

Table 3 contains the results in the cases of several children who were subject to recurrent vomiting. Several of these cases have been reported elsewhere recently.[6] The histories on which the clinical diagnoses were based will be found at the end of the paper. In all these cases the concentration of blood sugar fell to a far greater extent than in the normal control patients (table 2) and, in addition, acetone was present in the expired air in nearly all after the sixteen or eighteen hours of fasting, while in one or two the amount was strikingly large. The inorganic phosphorus is also apparently reduced to a greater extent than

6. Josephs, Hugh: Bull. Johns Hopkins Hosp. **37**:376 (Dec.) 1925. (Also footnotes 4 and 5.)

the normal, but, again, the number of observations is not sufficient to establish this point beyond any doubt.

COMMENT

Before commenting on the results of the study, I must define what I mean by hypoglycemia. That a blood sugar of 0.06 per cent is abnormally low would be accepted by the most critical; that one of 0.09 per cent is to be considered within normal limits is likewise unquestionable. Between these limits there is a gap in which values may be normal or abnormal, depending on the conditions under which they exist. If a child's habitual blood sugar is 0.100 per cent or higher, a blood sugar of 0.08 per cent may be abnormally low, but before one can make such an assertion, additional facts must be considered. In this child, 0.08 per cent becomes a normal value after two or three days of fasting; it can hardly be considered so after less than twenty-four hours of fasting. It is evident, then, that before a blood sugar value can be considered as either normal or abnormal, several additional facts must be considered. The habitual blood sugar under standard conditions must be known in order to determine the amount of the reduction in blood sugar concentration. Then a sufficient number of normal children must be studied under as nearly as possible identical conditions to determine the normal limits of the reduction of blood sugar.

It is going too far afield to enter into a critical discussion of the normal limits of the blood sugar concentration. It is enough that I define what I mean by hypoglycemia as I have used the term in this paper. The blood sugar concentration that obtains under standard conditions may be considered as a base line from which variations are measured and it is the extent of the variations with which I am concerned, not with the position of the base line. I may differ from others in what I consider "standard conditions," and elsewhere in this paper I have defined "standard conditions," namely, the child to be free of infection, the blood to be obtained four to five hours after a meal by pricking the finger, etc.

PROBLEMS

Several questions are suggested by these studies. The first that I will consider is of a clinical nature. With what proportion of the cases of recurrent vomiting is hypoglycemia associated? It is impossible to give a complete answer to such a question from the material at hand. The children who were taken into the hospital for study were carefully chosen on the basis of a typical history, or an observed attack such as to leave no doubt as to its nature, or the presence of convulsions during an attack, as described in a recent paper, or a definite period of fasting preceding the attack, or the history of postanesthetic acidosis. It so

happens that the children studied in more than one attack had some degree of hypoglycemia in all of them. S. E., in her first attack with convulsions, had a blood sugar concentration of 0.065 per cent; in a second attack without convulsions her blood sugar concentration was 0.077 per cent—hypoglycemia only in the sense in which I have defined the term. S. S. in one attack had a blood sugar concentration of 0.060 per cent, in the next attack 0.073 per cent, and in a third attack 0.081 per cent. Both the later values might be considered nearly normal for the period of time the patient had been without food. Other children whose clinical histories have certainly been quite similar to those of recurrent vomiting have had no lowering of the blood sugar whatever, and some have even had considerable hyperglycemia.

I cannot, therefore, say with certainty that hypoglycemia is the cause of recurrent vomiting in general. It is coincident with a considerable number of attacks, and children who give clinical histories of recurrent vomiting in certainly a large number of instances have some peculiarity of carbohydrate metabolism, as the result of which their blood sugar falls more rapidly than normal at the outset of a fast. That such hypoglycemia is responsible for some of the symptoms, such as drowsiness, acetone body excretion, and in severe cases convulsions, seems to be undoubted; that it is responsible for the vomiting is by no means proved.

A second question to be answered is: Why does the blood sugar fall more rapidly in children who are subject to recurrent vomiting than in normal children? There are certain theoretic points that offer an approach to the problem, and a consideration of them may bring us closer to a probable solution. For the explanation of the rapid fall in the blood sugar there are two possibilities. The first and less likely one is that the glycogen store is not sufficient to meet the ordinary needs of metabolism. This might easily be the case when the child is malnourished or suffering from a chronic infection, but a failure to store glycogen while in good health seems a rather remote possibility. There is, however, evidence of a more positive nature that failure to store glycogen is not the cause of the rapid fall of blood sugar. This evidence is found in the spontaneous recovery from the attacks of recurrent vomiting. Moreover, in the case of both L. S. and W. A. during the artificially caused hypoglycemia, continuance of the fast was accompanied by an increase in blood sugar concentration. In one subject, observed in the hospital, the blood sugar concentration was 0.073 per cent on the second day of the attack, and acetone was present in the expired air; the next morning the blood sugar concentration had risen to 0.082 per cent and the acetone was present only in traces; all this change had taken place in spite of the fact that the child had not

had food between the two determinations. If one still should hold to the belief that lack of glycogen store is the cause of the fall in blood sugar, one is forced to the conclusion that glucose must be derived from other noncarbohydrate materials. The protein is a possible source, but a determination of the nitrogen of the urine in the case of L. S. and of W. A. failed to show a rise in its excretion during the rise in blood sugar. That there may be other sources of sugar is, of course, within the bounds of possibility but, if so, they still remain to be discovered.

The second possible explanation for the fall in blood sugar is that the supply is temporarily unable to meet the demand; and, *a priori*, this seems to be the more likely explanation. The supply of blood sugar is regulated by the forces that control the mobilization of glycogen; the demand is regulated by the rate of metabolism of carbohydrate. By "metabolism of carbohydrate" I do not mean necessarily oxidation, but merely the chemical changes concerned in the removal of glucose from the blood stream whether such changes lead to eventual oxidation or not. Whether the fault is primarily a temporary failure to mobilize sufficient carbohydrate, or whether it is primarily an increase in the rate of metabolism it is not possible at present to say. If the latter, then one must either assume a carbohydrate metabolism continually above normal, or else that the rate rises on slight provocation and that the conditions of the test are sufficient to cause a rise. That might possibly be so during the first night spent in a hospital, especially before an operation, but some of the tests were made on children who had been in the hospital a considerable length of time, and some on children who were too young to be apprehensive over their stay in the hospital to a sufficient degree to affect their metabolism.

A third question of importance to be answered is, granted that there is a rapid fall in blood sugar in certain children at the onset of a fast, how will this fall be affected by infections, anesthesia, undue excitement, or any other condition that may initiate an attack of recurrent vomiting? I have attempted to answer this question in regard to anesthesia in a recent article.[6] In it I have brought forward evidence which shows that the rate of carbohydrate metabolism is temporarily increased following anesthesia in some and probably in all children, and that this increase is responsible for a reduction in blood sugar concentration which is greater than would normally occur for the same period of fasting. If such an increase in rate of oxidation of carbohydrate occurred in a child who could not mobilize his glycogen sufficiently rapidly, an excessive fall in blood sugar might easily take place. I must emphasize again here that I do not mean a complete failure to mobilize carbohydrate, but a failure to meet the immediate demands of metabolism. It could conceivably happen that the meta-

bolic rate might be increased so greatly that a normal child would be unable to meet the emergency. A. U. (reported in the paper on anesthesia) was apparently quite nearly enough normal to have avoided any attack of vomiting in the past, but her blood sugar dropped more rapidly than normal during the fast preliminary to anesthesia, as shown in table 3, and later her respiratory quotient showed a somewhat more prolonged rise than that of any other child studied. The result was an excessive drop in blood sugar, vomiting, drowsiness and a large output of the acetone bodies.

FEVER STUDIES

In the case of fever, my studies are at present incomplete. In pneumonia there is a fall in blood sugar of greater extent than the normal during a sixteen hour fast, and it seems reasonable to suppose that there is also an increase in carbohydrate metabolism occurring with the increase in total metabolism that takes place during an acute infection. Excessive exercise is among those conditions that increase metabolic rate, and in fact it has been shown that exhaustion, as in a marathon race, is capable of causing great reduction of blood sugar.[7] It is not a far fetched supposition that, at the bottom of more than a few attacks of recurrent vomiting, is an afternoon of hard play in conjunction with a scanty lunch or a late supper. As a pure conjecture, I would place the emotional influences in the category of those conditions in which an increase in the rate of oxidation of carbohydrate is a factor in the initiation of an attack of recurrent vomiting. But is it primarily because these children have an unstable carbohydrate metabolism that is too easily increased, or is it primarily because they are unable to move their carbohydrate from relatively inaccessible stores? That is a question for which at present I have no answer.

SUMMARY

Some, and in all probability a large proportion, of the attacks of recurrent vomiting are characterized by hypoglycemia, which develops rapidly and in some instances may reach a considerable degree. The rapidity with which hypoglycemia develops at the beginning of a fast is made the basis of a test for recurrent vomiting which can readily be applied between attacks. The mechanism of the hypoglycemia is discussed, as well as the part played by anesthesia, fever and other conditions, in initiating an attack of the disease.

---

7. Levine, S. A.; Gordon, Burgess, and Derrick, C. L.: Some Changes in the Chemical Constituents of the Blood Following a Marathon Race, with Special Reference to the Development of Hypoglycemia, J. A. M. A. **82**:1778 (May 31) 1924.

CASE HISTORIES

CASE 1.—S. J. D. was a girl, white, whose family and past history were negative.

Present Illness.—At 16 months of age the child had a short febrile illness at the onset of which she had a convulsion. She recovered quickly and remained entirely well for two months. On the evening of July 26, she seemed somewhat feverish and ate a scanty supper. At 9 p. m. she began to have generalized convulsions, which were repeated at frequent intervals until she was admitted to the hospital at 3 a. m., July 27. At that time she was practically in a state of coma, and was having almost continual convulsions. Two hundred cubic centimeters of 5 per cent glucose were given intravenously. Shortly afterward the convulsions ceased, breathing became regular and at 8 a. m. the child was sitting up and playing normally. No blood sugar studies were made at the time, but the promptness of recovery following the administration of glucose was so striking as to leave little doubt that the convulsions were due to hypoglycemia.

This case is not properly one of recurrent vomiting, since no vomiting occurred, but in a recent paper I have given reasons for considering convulsions of this nature to be closely allied to attacks of recurrent vomiting.

CASE 2.—B. G., a boy, white, had an unimportant family and past history.

Present Illness.—On March 31, 1925, at the age of 2 years and 10 months, the child seemed listless and did not eat well. The next day he began to vomit everything that was given, including water. The vomiting continued up to the time he was admitted to the hospital on April 3. At that time he was somewhat drowsy, and his slow deep respiration gave evidence of some degree of acidosis. He was given 5 per cent glucose by rectum and slowly improved, so that by the next day he was able to take fluids by mouth without vomiting. The blood sugar was not determined during the attack.

The only element of doubt in this case is due to the fact that there was no history of recurrent attacks, although the attack itself was quite typical.

CASE 3.—C. H. was a boy, white, whose family and past history were unimportant.

Present Illness.—Since the age of 2 years, the child had had attacks of severe headache, associated with vomiting and constipation lasting for about three days. During the attacks he vomited everything he took by mouth, and became at times drowsy and at other times delirious. The attacks commenced and ceased without warning, and it was impossible to determine any factor that was the immediate cause of the attacks. Between the attacks he was quite normal. At the time of writing, the boy was 8 years of age, and the attacks showed no sign of decreasing in frequency or severity. He was not observed in an attack.

CASE 4.—M. P., was a boy, white, whose family and past history were negative.

Present Illness.—At 7 years of age the child began to have headaches accompanied by vomiting, occurring every two or three months, and each attack lasting for two or three days. The attacks came on in the early morning without warning, and between attacks the boy was well. The headaches were like those of migraine, being one sided, and sometimes accompanied by the appearance of colors or flashes of light. At the time that his blood sugar was determined and found to be reduced after fifteen hours of fasting, he was suffering from a headache which soon subsided spontaneously. The case is included here because it appears to be an instance, rare in the experience at this clinic, of the relation between recurrent vomiting and migraine that was emphasized by the older writers on the subject.

CASE 5.—A. W., white, had a negative family history.

Two years previous to admission to the hospital the child underwent an operation, and following it vomited for three or four days. From the descrip-

tion given the attack was typical of the so-called "post-anesthetic acidosis," a condition that is closely related to recurrent vomiting. The history was not otherwise that of recurrent vomiting.

CASE 6.—S. S., a girl, white, had an unimportant family and past history.

Present Illness.—The attacks of vomiting began when the child was about 6 years old, and in the last three years she has had eight attacks. They are quite typical in their course. The exciting cause could not be determined in the majority of the attacks. During the course the child vomited everything, became quite drowsy, lost weight rapidly and excreted acetone bodies in amounts much in excess of the amounts excreted in starvation. In two attacks she had hyperpnea, and at both these times the carbon dioxid capacity of the serum was about 30 per cent by volume. Her blood sugar concentration was determined late in three separate attacks, and it is of interest that as she grows older there is less reduction in the blood sugar.

INFLUENCE OF ACIDIFIED MILK ON DUODENAL FUNCTION IN INFANTS*

LLOYD ARNOLD, M.D.
CHICAGO

For the past seventy years,[1] at least, some form of acidified milk has been used by pediatricians in feeding babies. There have been many explanations given for the beneficial results that have been obtained. Most of these explanations were based on some theory of influencing gastric function:

1. That acidified milk acts by increasing the bactericidal properties of the gastric contents.[2]

2. That it causes a greater secretion of gastric juice.[3]

3. That it influences pancreatic function, and many other explanations.

In 1875, Uffelmann[4] mentioned that the titrable acidity of infant's stomach was much less than that of the adult, and was much lowered, or even absent, in babies with diarrhea. Allaria[5] was the first to determine the hydrogen ion concentration of the gastric contents of infants. He records an average of p_H 5.3 for bottle fed babies. Davidsohn,[4] as well as Marriott and Davidson,[6] have investigated this question thoroughly. They report a hydrogen ion concentration of p_H 3.75 in the gastric contents of normal breast fed infants, p_H 5.1 after cow's milk feeding, and p_H 3.71 after whole lactic acid milk was fed. These workers report a decrease in acidity of the gastric contents of infants suffering from infectious and nutritional disorders.

---

* Received for publication, Jan. 4, 1926.

* From the Department of Bacteriology, Pathology and Preventive Medicine, Loyola University School of Medicine.

* Read in abstract form before Central States Pediatric Society, Chicago, Nov. 6, 1925.

1. Ballot, A. M.: Nederl. Tidjschr. v. Geneesk., 1865, p. 402.

2. Leichtentritt, B.: Ueber Buttermilchwirkung, Jahrb. f. Kinderh. **94**:119, 1921.

3. Dehnal, E.: Ueber die Wirkung der Buttermilch auf die Magensekretion, Monatschr. f. Kinderh. **27**:58, 1924.

4. Uffelmann, quoted by Davidsohn, H.: Beitrag zur Physiologie und Pathologie der Magenverdauung beim Säugling, Arch. f. Kinderh. **69**:239 (April) 1921.

5. Allaria: Untersuchungen ueber Wasserstoff—Ionen—Konzentration im Säuglings Magen, Jahrb. f. Kinderh. **67**:123, 1908.

6. Marriott, McK., and Davidson, L. T.: Acidity of the Gastric Contents of Infants, Am. J. Dis. Child. **26**:542 (Dec.) 1923.

Marriott in America and Mueller [7] in Germany have called attention to the part played by buffer substances in the food on the hydrogen ion concentration of the infants' gastric contents.

The gastric contents that pass into the duodenum are, under physiologic conditions, acid in reaction. The secretions from the digestive glands that empty into the duodenum are alkaline in reaction. The external pancreatic secretion is the most alkaline of this group,[8] ranging from p_H 7.17 to 8.85. The hepatic bile is more alkaline than the cystic bile, but neither is so alkaline as the pancreatic juice.[9] The secretions from the duodenal glands and the mucosa of the duodenum are slightly alkaline in reaction. The hydrogen ion concentration of the contents of the upper part of the small intestine, therefore, depends on the gastric, pancreatic, hepatic and intestinal secretions. The gastric secretions contain the acid radicals and the pancreatic juice is the main source of alkalis.

McClendon and his co-workers [10] have shown that the duodenum of infants, and the small intestine of puppies, dogs, cats, and suckling rabbits are acid in reaction. Moro and his co-workers [11] have pointed out that the infant's small intestine is acid in reaction from the duodenum to the middle or lower part of the jejunum. The portion with the acid reaction is relatively free of bacteria, but when the alkaline reaction begins, the bacterial flora is considerably increased.

INTESTINAL FUNCTION OF DOGS

We have recently described an experimental method of studying some phases of the intestinal function of dogs.[12] Briefly, the preparation is as follows: By means of a ventral midline incision, a portion of the small intestine to be studied is attached to the intact anterior abdominal wall, lateral to the line of incision. In some cases several segments have been attached at various levels from the duodenum to the cecum. The incision is then closed and allowed to heal. We can then enter the segment with a needle, and aspirate material for bacteriologic and chemical study into a syringe. A refinement of technic has given us good preparations, the dogs were normal, and there was no evidence

7. Mueller, F.: Ueber das Pufferungs Vermögen der Kuhmilch, Ztschr. f. Kinderh. **35**:285 (June) 1923.

8. Gyotoku, K.: Beitrage zur experimentellen Physiologie und Pathologie der Sekretion des Pancreas Saftes, Mitt. a. d. med. Fakult. d. k. Univ. zu Tokyo, **30**:409, 1923.

9. Okada: On the Reaction of the Bile, J. Physiol. **50**:114, 1915-1916.

10. McClendon, J. F.; Bissell, F. S.; Lowe, E. R., and Meyer, P. F.: Hydrogen Ion Concentration of Contents of Small Intestines, J. A. M. A. **75**:1638 (Dec. 11) 1920.

11. Hahn, H.; Klocman, L., and Moro, E.: Experimentelle Untersuchungen zur endogenen Infektion des Duenndarms, Jahrib. f. Kinderh. **84**:10, 1916.

12. Arnold, Lloyd: J. Infect. Dis. **38**:246 (March) 1926.

of abnormal function. The table gives the average bacterial flora and hydrogen ion concentration in the various levels of the intestinal tract of a normal young dog.

Bacterial Flora and Hydrogen Ion Concentration of the Small Intestine (Post-Digestive) of Healthy Dogs

Portion of Small Intestine	Bacterial Flora	Hydrogen Ion Concentration
Duodenum	Few gram positive cocci	p_H 5.2 to 6.0
Jejunum, upper half	Few gram positive cocci	p_H 5.5 to 6.5
Jejunum, lower half	Gram positive cocci, few gram positive and gram negative bacilli	p_H 6.0 to 7.0
Ileum	Very rich bacterial flora	p_H 6.8 to 8.0

Carlson,[13] Salle,[14] and others have shown that a disturbance of the heat regulatory mechanism of the body is accompanied by a depression of gastric secretory function. These workers used dogs in which the Pawlow pouch operation had been performed and elevated the animal's temperature by increasing the external temperature and by injection of foreign proteins. Where fever is present, there is a depression of gastric secretion. This has been found by all investigators in this field. Moro[15] found a pure culture of *B. coli* in the duodenum of infants with dyspepsia with fever, regardless of the character of the bacteria in the feces. Many observers have substantiated this observation.

METHOD

We have caused an elevation in the body temperature of dogs with a ventral fixation of the duodenum. This has been done by the subcutaneous injection of either typhoid, coli, or staphylococcus vaccines, and also by confinement within a warm room. In every instance we have found that the bacterial flora of the duodenum changed to the characteristic type found normally in the ileum, a rich flora with *B. coli*—aerogenes group predominating. The hydrogen ion concentration changed to near neutrality (p_H 6.8 to 7.4). This usually occurred from one to two hours before the *B. coli* appeared in the duodenum, but we found this time factor variable with the same dog at different times, and with different dogs at the same time—after meals, etc. This change in reaction must be due to depressed gastric secretion. Gyotoku[8] has shown that the pancreatic juice does not change appreciably in amount

13. Meyer, J.: Cohen, S. J., and Carlson, A. J.: Contributions to the Physiology of the Stomach, Gastric Secretion During Fever, Arch. Int. Med. **21**:354 (March) 1918.

14. Salle, V.: Die Einwirkung hoher Aussenlufttemperaturen auf die Sekretorische Taetigkeit des Magens, Jahrb. f. Kinderh. **74**:697, 1911.

15. Moro, E.: Bemerkungen zur Lehre von der Säuglings Ernaehrung, Die Endogene Infektions des Dünndarms, Jahrb. f. Kinderh. **84**:1, 1916.

or constituents as a result of a disturbance of the heat regulatory mechanism in dogs.

We injected alkaline buffered phosphate solutions directly into the duodenum.[13] This is followed by a leukocytosis that appears in from twenty to thirty minutes and lasts from three to six hours. There is an increase of two or three times the normal number of leukocytes in the peripheral circulation. Between one and two hours after the alkaline buffer is injected into the duodenum, the flora is the same type as found in the ileum or cecum. These results have been obtained repeatedly on several dogs. In fact, we have never been able to produce a neutral or alkaline reaction in the duodenum or upper jejunum of the dog without causing a change in the flora. The temperature is variable; some dogs show an elevation of 1 or 2 F.; others have a normal temperature.

The normal regulatory mechanism for the control of the bacterial flora within the lumen of the duodenum and upper half of the jejunum of the dog does not function in an alkaline environment. Experimentally, we can change the normal acid reaction (p_H 5.0 to 6.0, average p_H 5.5) to an alkaline or neutral reaction by elevation of the temperature of the animal.

Zahn[16] found that the secretory activity of the stomach was not changed in the normal dog with a duodenal fistula by feeding buttermilk. He records that a dog with fever had a lowered hydrochloric acid secretion and a rapid emptying time when cow's milk was fed, but the buttermilk was retained for the normal length of time. He attributes this to the acid content of the milk. Schiff and Gottstein,[17] working with a normal dog with a duodenal fistula, found that the hydrogen ion concentration of the duodenal contents was the same after cow's milk (p_H 6.59) and acid milk (p_H 3.46) were fed. In other words, the acidity of the diet did not affect the normal hydrogen ion concentration (p_H 5.46 to 6.25) of the duodenum.

We have mentioned elsewhere[13] the difficulties encountered in working on dogs with a duodenal fistula. These dogs are never normal, usually there is an elevation of temperature and we have always found leukocytosis present. We attribute these evidences of abnormal physiology to dehydration and digestion or autolysis of the areas of tissue in contact with the fistulous opening. Chart 1 shows a graph of the hydrogen ion concentration of material obtained from a duodenal fistula (third part of the duodenum). At the time of the experiment, this dog

16. Zahn, K. A.: Ernahrungversuche am Fistelhund, Jahrb. f. Kinderh. **96**: 259, 1921.

17. Schiff, E., and Gottstein, W.: Wie verhält sich die Azidität des Duodenalinhalt bei Verabreitung von sauren Milchmischungen ? Jahrb. f. Kinderh. **107**:99, 1925.

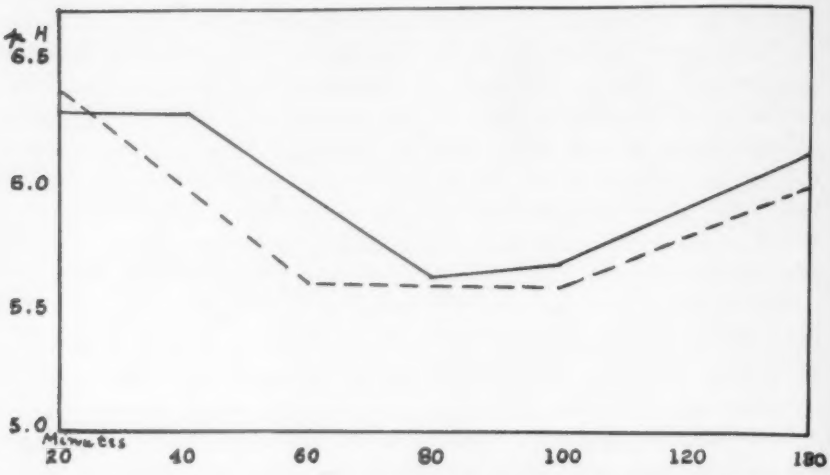


Chart 1.—Hydrogen ion concentration of material obtained from duodenal fistula of normal dog after feeding. Straight line, whole cow's milk (p_H 6.4); broken line, lactic acid milk (p_H 5.0).

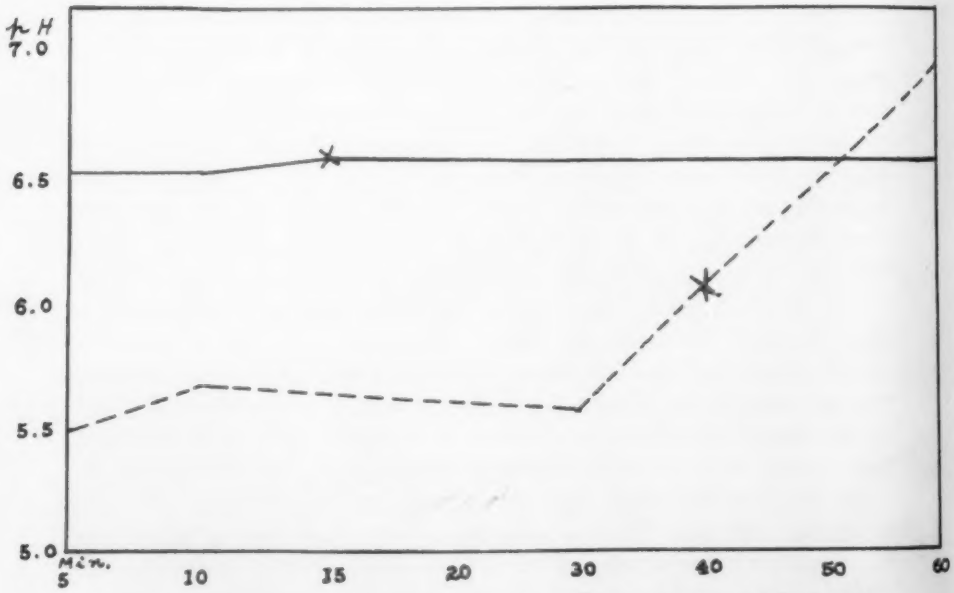


Chart 2.—Hydrogen ion concentration of material obtained from duodenal fistula of dog, with elevation of temperature (102.8 F.) after feeding. Straight line, whole milk (p_H 6.4); broken line, lactic acid milk (p_H 5.0).

had a normal temperature (101.3 F.), but the leukocyte count was 20,500. Whole cow's milk and lactic acid whole cow's milk were fed. These dogs are always so dehydrated that it is unnecessary to use a stomach tube to induce them to take fluids. The first material noticed in the container was twenty minutes after the meal; the last material, of opaque milky color, appeared one hundred and twenty minutes after the meal. The graph shows little difference between the hydrogen ion concentration of the duodenal contents of whole cow's milk and lactic acid milk. This supports Schiff and Gottstein's observation. Chart 2 is the same experiment, in graph form, six hours after the injection of a bouillon cultured with staphylococcus vaccine. The temperature was elevated and the leukocyte count was 31,200. The whole milk had a hydrogen ion concentration of p_H 6.4. The duodenal contents were p_H 6.5. The stomach started emptying in five minutes and was completely empty in fifteen minutes. The lactic acid milk had a hydrogen ion concentration of p_H 5.0. The duodenal contents had a normal reaction (p_H 5.5) from the beginning of the emptying of the stomach (five minutes after feeding) until ten minutes before the last trace of milky colored material appeared in the duodenum. This was forty minutes after feeding. The duodenal reaction rapidly became neutral after the lactic acid milk was passed out of the stomach. This is a partial substantiation of Zahn's work. But the dog with a duodenal fistula is pathologic and not physiologic. Results are always variable, and to draw analogies from such preparations is a dangerous procedure. Demuth,[18] for instance, made 176 fluoroscopic examinations on fifty-two babies, and could not demonstrate a great difference between cow's milk mixtures and sour milk mixtures on the emptying time of the stomach.

HYDROCHLORIC ACID SECRETION

The physiologic mechanism of hydrochloric acid secretion in the stomach is too complicated, and is dependent on too many factors to expect that there would be a gradual diminution curve that would correspond to a temperature elevation curve. There are great variations of hydrochloric acid secretion within the physiologic range. The baby's nourishment is derived from aqueous solutions and suspensions of food materials. On mother's milk the gastric contents is saturated to the full buffer capacity (p_H 3.5). On whole cow's milk all of the buffers are not saturated (p_H 5.0). The material passing into the duodenum from the stomach is different under the two conditions. The same decrease in the hydrochloric acid on feedings with mother's milk would not be so liable to allow unbuffered material to enter the duodenum as would be the case with feedings of cow's milk.

18. Demuth, F.: Magenfunktions Prüfungen beim Kranken Säuglings, Monatschr. f. Kinderh. **24**:418 (Jan.-Feb.) 1923.

The only source of acid radicals in the upper part of the small intestine comes from the stomach. This is not in the form of free hydrochloric acid, but of hydrogen ions bound onto buffers in the gastric contents. The alkaline hepatic, pancreatic, and intestinal juices mixing with this acid buffered gastric contents constitutes the contents of the duodenum and jejunum. The maintenance of a slightly acid reaction (from p_H 5.0 to 6.0) is dependent for the most part on gastric secretion.

In case of an elevation of temperature in a baby who is bottle fed, it would be logical to expect a decrease in hydrochloric acid secretion in the stomach, and it would be advisable to decrease the buffers in the milk to compensate for the lack of acid. This would allow gastric contents to be maintained at a reaction nearer normal, and would not allow unbuffered or almost neutral material to be passed into the duodenum. This should decrease the incidence of nutritional disorders following fever conditions. Dr. R. A. Black has been using this as a preventive for about eighteen months. His results so far are encouraging. While this work has been in progress, Ylppö [19] in Sweden and Demuth [20] in Germany have reported the use of the same process, with excellent results.

COMMENT

The use of buttermilk, lactic acid milk, protein milk and such mixtures, influence duodenal function more than they do gastric function. We do not yet know the amount of actual hydrolysis of protein due to peptic activity in the infant's stomach. The evidence at present available substantiates our conception of gastric function in the baby as being an important chemical mechanism, as it maintains a constant duodenal and jejunal reaction that allows the physiologic process of control of the bacterial flora of this region of the intestinal tract.

So far as we now know, this upper part of the small intestine is almost free of bacteria, and when a rich bacterial flora is present the reaction is neutral or alkaline. This is dependent on a depressed gastric secretion, or, a better way of putting it, dependent on the entrance into the duodenum of material that does not contain enough acid radicals to maintain the proper hydrogen ion concentration in the presence of the alkaline secretions entering the lumen of the intestinal tract. This brings about the nutritional disturbances, Moro's endogenous infections, etc.[21]

---

19. Ylppö, A.: Ueber den Einfluss Mechanischen und infektiösen Fiebers auf die Acidität des Mageninhalt bei Säuglingen, Acta Pediat. **3**:213, 1924.

20. Demuth, F.: Salzsäure Prophylate und Therapie der Dürchfalle bei Fieberhaften Erkrankungen der Säuglinge, Klin. Wchnschr. **3**:985 (May 27) 1924.

21. Davison, W. C.: The Bacteriology of Diarrhea in Infants, South. M. J. **17**:552 (Aug.) 1924.

It is well known that calcium salts can stay in solution in an acid medium only. There is no evidence available showing that calcium is absorbed from the stomach. Its absorption, then, depends on duodenal reaction; if it is normal, gastric function is normal. The whole question of infant tetany, rickets, and other such problems, can be reviewed from a different angle.[23]

---

23. Gamble, J. L., and Ross, G. S.: The Effect of Ingestion of Hydrochloric Acid Producing Substances on the Acid-Base Metabolism of an Infant and the Probable Manner of Their Action in Treatment of Tetany, Am. J. Dis. Child. **25**:470 (June) 1923. Steinbach, H.; Hart, E. B.; Sell, M. T., and Jones, J. H.: The Availability of Calcium Salts, J. Biol. Chem. **56**:375 (June) 1923. Babbott, F. L.; Johnston, J. A., and Haskins, C. H.: Gastric Acidity in Infantile Tetany, Am. J. Dis. Child. **26**:486 (Nov.) 1923.

GOITER IN CHILDREN IN NEW YORK CITY

THYROID SURVEY OF 11,084 SCHOOL GIRLS AND 783 SCHOOL BOYS *

FRANCES COHEN, M.D.
NEW YORK

During the past two decades, iodine in its relation to the thyroid gland and to the prevention and cure of goiter has been a subject of renewed interest and investigation. The work, especially that of Marine and his associates,[1] has demonstrated that simple goiter can be prevented, and has stimulated the undertaking of thyroid surveys in many parts of the world.

GENERAL OBSERVATIONS

Marine [2] states that goiter is a term used to describe all thyroid enlargements in animals as well as in man. Although the ultimate cause of thyroid enlargement is still unknown, it is immediately dependent on a relative or absolute deficiency of iodine in the thyroid gland—iodine hunger. This hunger exists if the iodine content of the thyroid gland falls below one-tenth of 1 per cent (0.1 per cent),[3] and is made evident by the symptom of a slight compensatory swelling or hyperplasia of the gland, to which the term simple colloid goiter has been applied. Simple goiter includes all those enlargements formerly grouped as endemic, epidemic, sporadic and physiologic.[2]

The main sources of iodine in nature are milk, cereals, leafy vegetables, some fruits, and water derived from nongoitrous regions. Sea salt, seaweed, sea foods and sea water are especially rich in iodine. The air near the sea coast also supplies a small amount. As a result of the studies of McClendon and Hathaway,[4] we know that in nongoitrous regions, such as the coast of New England or California, the iodine content of the food may be 100 per cent higher than that in goitrous regions.

Goiter is associated with districts of glacial formation in contradistinction to districts of nonglacial formation. Districts of glacial forma-

* Received for publication, Jan. 6, 1926.

1. Marine, Lenhart, Kimball and Rogoff: The Prevention of Simple Goiter, Bull. 26, Western Reserve University, July, 1923.

2. Marine, David, and Kimball, O. P.: The Prevention of Simple Goiter in Man, J. Lab. & Clin. Med. **3**:40-48 (Oct.) 1917.

3. McClendon, J. F., and Williams, Agnes: Simple Goiter as a Result of Iodine Deficiency, J. A. M. A. **80**:600 (March 3) 1923.

4. McClendon, J. F., and Hathaway, J. C.: Inverse Relation Between Iodine in Food and Drink and Goiter, Simple and Exophthalmic, J. A. M. A. **82**:1668 (May 24) 1924.

tion contain less iodine in the soil and in the water supply than do districts of nonglacial formation, because the soluble sodium salts of iodine have been removed by the melting ice.[5]

The goitrous area in the United States is that part of the country which was covered by the three great ice sheets, the lower border of which extended from the eastern part of New York State, south below Cincinnati and nearly to the Pacific coast.[4]

The relative infrequency of simple goiter along sea coasts and its mild type when present, is mentioned in most treatises on the subject. It is especially brought out in "Defects Found in Drafted Men," United States War Department, 1920, p. 323, in which the ratio stands as 1.02 to 17.55, when sea coast dwellers are compared to dwellers in mountain regions.

GOITER SURVEYS

Following the suggestion of Dr. Marine that it was necessary to ascertain the incidence of goiter in representative units of the population in various parts of the United States, numerous surveys have been made in widely separated districts here and abroad, especially in goitrous regions. The findings of a few of the more important of these surveys are indicated in table 1.

It is now generally accepted that the incidence of goiter increases in a district of glacial formation from the periphery of the district toward its center because the iodine supply in the soil is less in the center than at the periphery.[6] Hence the incidence of goiter is less in Cincinnati near the southern margin of the glacial formation (32 per cent) than it is in Michigan (47.2 per cent), the center of the glacial region.

ETIOLOGY OF SIMPLE GOITER

Simple goiter is especially apt to occur at three periods of life, namely, (1) fetal life, (2) puberty and (3) during pregnancy. Marine states that "Thyroid hyperplasia, goiter, is a compensatory reaction arising in the course of a metabolic disturbance and immediately dependent on a relative or absolute deficiency of iodine." This deficiency may be brought about in the following ways:[7]

1. The actual intake of iodine may be below the normal amount needed to meet the ordinary demands of thyroid activity at any time of life—to say nothing of the additional demands made at the time of puberty, pregnancy or by infections or other morbid states.

---

5. Hayhurst, Emery: Simple Goiter—An Iodine Starvation Disease, Ohio Conference on Water Purification, Third Annual Report, pp. 76-82, State Dept. Health, Nov. 21-24, 1923.

6. McGarrison, Robert: The Thyroid Gland in Health and Disease, London, Ballière, Tindall, Cox, 1917.

7. Marine, David, and Kimball, O. P.: The Prevention of Simple Goiter in Man, J. A. M. A. **77**:1068-1070 (Oct. 1) 1921.

TABLE 1.—*Goiter Surveys*

Authority	Location	Number Examined	Incidence in Percentage			Ages	Remarks
			Children	Girls	Boys		
Klinger (Schweiz. Kropfk. 1922, 1923)...	Switzerland, St. Gallen....	.....	87.6	....	....	.....	1919 incidence 87.6%; 1922 incidence only 13.1%, due to prophylaxis as public health measure
F. De Quervain (Tr. by J. Snowmon, London, John Bale, Sons and Danielsson, 1924)	Switzerland, Berne.....	7,500	73.2 93.7	....	15.0	7 to 15	Fairly liberal standards
Marine and Kimball [2].....	Ohio, Akron.....	3,872	....	56.41	....	10 to 20	Precise standards
Olesen (Cincinnati Pub Health Rep. [July] 1924)	Ohio, Cincinnati.....	47,493	32.0	39.8	26.6	6 to 17	Greatest prevalence between 11 and 13 years; one frank case of exophthalmic goiter; three tentative cases
Olin (J. A. M. A. **82**: 1328 [April 26] 1924)	Michigan, 4 counties.....	31,612	47.2	53.8	40.5	5 to 18	Liberal standards used; only visible glands included
Olesen and Clark (Pub. Health Rep. [Oct. 10] 1924)	Minnesota.....	4,061	57.9	71.0	40.9	5 to 23	Precise standards
Clark and Pierce (Pub. Health Rep. **29**: 939, 1914)	West Virginia.....	13,836	....	8.91	....	School children	
Clark	Virginia.....	6,432	12.7	12.6	0.1	School children	
Foard (Pub Health Rep. **39**: 2354, [Sept.] 1924)	Montana, 7 counties.....	13,937	21.6	32.0	13.4	6 to 20	Liberal standards; only distinctly enlarged glands included
Wallace (California & West. Med. **22**: 431, 1924)	Utah.....	69,256	42.7	54.3	30.0	5 to 20	Elementary and high schools; precise standards
Porter	Utah University.....	1,945	....	56.6	31.2	College age group	Tendency to increase with age in goitrous centers; larger per cent of moderates and marked enlargements found
Hall, Hofrichter and Mohr (Endocrinology **9**: 137, 1925)	Washington, Seattle.....	3,160	39.3	43.4	35.5	6 to 15	Precise standards
Palmer (J. A. M. A. **82**: 1568 [May 10] 1924)	New York, Syracuse.....	25,875	18 0	....	....	.....	High school pupils, 20 per cent; grammar school pupils, 16 per cent

Olesen (Pub. Health Rep. **40**: 1, [Jan.] 1925)	Colorado, Denver.....	9,656	....	27.3 (white) 26.3 (negro)	....	8 to 22	Precise standards
Olesen	Colorado, 4 counties.....	1,762	....	73.4	53.3	9 to 20	
Klein (München. med. Wchnschr. **72**: 1244, 1924-1925)	Germany, Essen.....	8,033 1,448 12-13 yrs.	....	57.9	54.5	12 to 13	
Lewis (Semana med. **2**: 713, 1924).....	South America, Argentina	.....	50 to 98.11	....	....	3 to 15	
Lewis	Venezuela, Buenos Aires...	.....	86 to 88	....	....	.....	
Kraeuter (München. med. Wchnschr. **69**: 47, 1922)	Bavaria, Munich.....	1,840	....	56.0 62.5	....	3 to 19 14 to 15	
Schroetter (Wien. klin. Wchnschr. **38**: 72, 1925)	Austria: Vienna, Linz, Salzburg, Graz, Klangenfurt, Innsbruck	.....	55.40	59.6	51.0	6 to 15	
Lamel (Med. Klin. **20**: 112, 1924).....	Germany, Berndoff.....	.....	....	46.0	....	School children	
Guilder (Ann. Clin. Med. **1**: 248, 1923)..	Illinois University (15 states represented)	609	....	45.3 66.0	....	16 to 30 at 16 yr.	Entering students, class 1924; group between 27 to 30 years showed no enlargements
Luck (J. Indiana M. A. **17**: 183, 1925)	Indiana University.....	.....	....	41.0	....	17 to 18	Freshman class
Hall (Northwest M. J. **6**: 189, 1914)....	Washington University....	3,339	....	30.98	17.93	19 to 20	Older age group
Levin (Arch. Int. Med. **27**: 421, 1921)..	Great Lakes Region.....	1,783	63+	....	....	1 to 60	Unselected persons; some degree of incidence in any age group; at second, 32 per cent; at 18 years, 89 per cent
Olesen (Illinois M. J. **27**: 16, 1915)....	Great Lake Basin.....	800	....	17.8	6.7	.....	Liberal standards; only moderate enlargements included
Cannavan (Am. Phys. Ed. Review **27**: 621, 1912)	Massachusetts, Wellesley College	.....	....	16.0	....	.....	Older group; recruited from all over the country
Blankenship (Wisconsin M. J. **19**: 561, 1920-1921)	Wisconsin University.....	13,796	28.0	41.0	21.9	Average age 19.9 yr.	Entering students from 1910 to 1917; exophthalmic goiter, 93 cases (0.6%); girls, 1.2 per cent; boys, 0.29 per cent

It is this condition which prevails among the inhabitants in so-called endemic goitrous centers, marked glacial districts, and explains why a large proportion of men and women, boys and girls of all ages have thyroid disturbances, ranging from mild to very severe types, including cretinism and congenital goiter. The animals are also goitrous.

2. The actual intake of iodine may be the normal amount needed to meet the ordinary demands of life of the great majority of people, but not enough in given persons to enable their thyroid glands to respond to the additional physiologic demands of puberty or of pregnancy, or to the pathologic demands made by infections, intoxications or anemias, or by injury to the sex glands or the suprarenal cortex. In addition, the metabolism of a diet rich in fat and proteids, by throwing additional work on the thyroid may produce a relative insufficiency of iodine. These are the conditions which largely explain the occurrence of sporadic cases of goiter in nongoitrous regions, rich in iodine.[8]

3. The actual intake of iodine is the normal amount needed, but the supply to the thyroid gland is diverted by certain factors, such as intestinal *Metazoa,* amebae and tapeworms.

COMPARATIVE INCIDENCE OF THYROID ENLARGEMENT IN MEN AND WOMEN

Thyroid enlargements occur about three times more frequently in women than in men, but the ratio is a constantly varying one. As the center of a goitrous region is approached, the ratio becomes more nearly equal, due mainly to fetal involvement. In certain goiter centers in Switzerland, the ratio is 1.6 women to 1 man, and in the Himalayas it is 1 to 1.[6] Therefore, the incidence of goiter in men and boys is an important index of the degree to which a definite region is goitrous.

THE NORMAL THYROID—CAN IT BE PALPATED?

There is no hard and fast division between the size of the normal and of the goitrous thyroid. Hunziker[9] states "that the size of the normal thyroid is not known, and for that reason no one can state where the normal thyroid gland stops and goiter begins. Even when the normal adult size is theoretically established, the normal adult sizes

---

8. Foreign Letter: Present Status of the Problem of Endemic Goiter, J. A. M. A. **84**:997 (March 28) 1925.

"Simple goiter must be sharply distinguished from exophthalmic goiter. So far as is known, there is no necessary association or etiologic relationship between the two conditions" (Marine and Kimball). Prof. F. de Quervain of the University of Berne states: "It is just in those countries which are free from goiter that the worst cases of exophthalmic goiter are found."

9. Hunziker, Heinrich: Die Prophylaxe der Grossen Schilddrüse Ein Stuck Vergluchende Klimatologie der Schweiz und Ein Leitfaden für Systematische Naturwissen—Schaftliche Forshungen, Leipsic, 1924.

at different ages and in various parts of the world are not known." Hertzler [10] says that ordinarily in average necks the normal thyroid gland is just palpable to experienced hands. Cabot [11] maintains that the normal thyroid can rarely be felt. The normal thyroid gland is larger in girls than in boys.

It is clear from what has been said that the standard adopted in a thyroid survey is an arbitrary one, and that the unit of measure, so to speak, has not been accurately established. This suggests to me that in surveys in which precise standards have been used, there may be a large group of glands reported as slightly enlarged, and not visibly enlarged, that constitute a borderline, preclinical group, so to speak, which possibly may fall within the limits of normality when more scientific and accurate standards have been established through a greater knowledge of the life history of the gland in the sexes at different ages, and in different races, peoples and climates.

The Michigan survey, for example, has taken account of this difficulty, and in its report classifies none but visibly enlarged glands as enlarged thyroids. In spite of eliminating the doubtful group, the Michigan survey shows an incidence of 53.8 per cent of enlarged thyroids in girls.

THYROID INVESTIGATIONS IN NEW YORK CITY PRIOR TO 1924

New York City is at the very margin of the ice sheet, the glaciated area, but because of its location on the sea coast, it has a good supply of iodine in the air and in the available sea food, and therefore one would not expect to find a high incidence of goiter. Its water supply is classed by J. F. McClendon as rich in iodine—the Catskill supply containing 110 parts of iodine per hundred billion parts of water; the Croton supply, 130 parts and the Long Island supply 250 parts.

Contrast these figures with those which obtain in endemic goitrous centers: Marquette, Michigan, 2; Mt. Clemens, 7.6; Portland, Oregon, 10; Chicago 12, and Columbus, Ohio, 21 parts of iodine per hundred billion parts of water.[4]

In spite of the fact that one would not expect to find a considerable incidence of goiter in New York City, in 1917, the New York City Department of Health made a survey of the thyroid condition of about 3,000 girls in the Washington Irving High School, and each year for the last four years a survey has been made. From 3 to 4 per cent were found to have some degree of enlargement of the gland. The standards used were liberal.

Again, in 1922, the Board of Health examined 5,000 children in its mercantile offices and found twenty boys and sixty-four girls ranging

10. Hertzler, Arthur E.: Diseases of the Thyroid Gland, St. Louis, C. V. Mosby Co., 1922.

11. Cabot, R. C.: Physical Diagnosis, 1923, p. 34.

between 14 and 16 years of age presenting some degree of thyroid enlargement.

Dr. Joseph C. Horan, Chief Medical Examiner of the Metropolitan Life Insurance Company, has made a very careful study of the thyroid condition of 7,500 of the women employees mainly between the ages of 20 and 30 years. The standards used in the survey were very precise. The study shows an incidence of less than 3 per cent of enlarged thyroids in this older age group.

THYROID SURVEY OF 11,084 SCHOOL GIRLS AND 783 SCHOOL BOYS IN NEW YORK CITY

Another thyroid survey of school girls in New York City was made during April and May, 1924, by the Department of Physical Training and Educational Hygiene, Board of Education, New York City. Later, in 1924, a supplementary survey of 783 school boys in Manhattan was made by me.

The purpose of the study undertaken by the Department was to determine the incidence of goiter in school girls of New York City, the type of goiter, whether mild or severe, and to make appropriate recommendations, if necessary, for its control and treatment.[12]

At a conference, preliminary to starting the thyroid survey, the technic of the examinations and the diagnosis were standardized.

It was decided to adopt Dr. Marine's classification and methods, with slight modification, and the thyroid glands in this survey were examined from the standpoint of normal, slight, moderate and marked enlargements.[2] The pupils were also examined for gross signs of exophthalmic goiter. No observations were made to discover persistent thyroglossal stalks, nor to examine tonsils or teeth for infection. An effort was made to correlate the activity of the menstrual cycle and the establishment of the menstrual function with the condition of the thyroid gland.

An effort was also made to correlate the number of years of residence of the girl in New York City or in other places, and the birthplace of the mother, with the thyroid condition. This table, however, is omitted in this study because it does not include the correlation of age, an important factor in the incidence of thyroid enlargements. A study of the thyroid condition of negro girls was also attempted for comparison with white girls.

Chart 1 shows the form that was used for recording the findings of this study.

Under normal are included all glands (*a*) which are not visible as a bulging of the skin across the trachea, (*b*) which have on palpation

12. The examination of the girls as reviewed in this paper was carried out by Dr. I. H. Goldberger in the Bronx, and by me in Manhattan. I later examined the group of 783 Manhattan boys.

a barely detectable band of thyroid tissue across the trachea (the thyroid isthmus) and (*c*) lobes either not palpable or barely palpable.

Those with enlarged thyroids have been divided into three arbitrary groups: (1) slight, (2) moderate and (3) marked enlargements.

1. Slight: Under slight have been grouped those subjects with (*a*) visible bulging of the skin over the thyroid isthmus (not due to fat deposit), (*b*) a widened or thickened isthmus band or mass on palpation and (*c*) readily palpable lobes.

No. 1 15M 3-24 Thd.

BOARD OF EDUCATION OF THE CITY OF NEW YORK

DEPARTMENT OF PHYSICAL TRAINING AND EDUCATIONAL HYGIENE

P.S. Bor.		Grades	Dates
Name	Race	City	State
Age	Birthplace of Child		
	Father		
	Mother		
Years in N. Y. City	Previous Residence		

0 Normal				2 Moderate				Tract			
1 Slight				3 Marked				Rec. Illness			
Exopthal				Tremor				Mottling			
M. Present				Due one week				Never			

Chart 1.—The conditions under which the survey was carried on in Manhattan rendered it impossible to interpret correctly the significance of tremor, mottling, etc. Hence the recording of these symptoms in the Manhattan group were discontinued early in the study.

2. Moderate: Under moderate enlargements have been grouped those with "gross deformity," as shown by lateral bulging of the neck and by marked bulging of the skin anteriorly, from the enlarged isthmus.

3. Marked: Under marked enlargements are grouped those with still greater deformity. In the Manhattan group there was no case of excessively marked deformity.

The method of examination was to inspect the pupil in a good light; to follow the inspection by palpation of the isthmus and the lobes and to palpate again, in all doubtful cases, as the pupil swallowed.

The standard for normal adopted in this survey, which is Dr. Marine's standard, is a much more precise standard so far as I know, than that adopted in many thyroid surveys. In the Michigan survey, all subjects, boys and girls, who did not present visible thyroids

were placed in the normal group. The Swiss goiter commission also apparently uses a less precise standard. Hence it is possible for the findings in this survey to be only approximately compared with the findings in other surveys, in which more liberal standards were employed.

COMMENT

A total of 11,084 girls were examined, 6,225 in Manhattan, 4,654 in the Bronx and 205 pupils from miscellaneous high schools. Of these, 9,978 belonged to the white race and 1,106 to the negro race. The total group was thought to be a representative cross section of the population.

The survey included an attempt to compare the thyroid condition in the white and in the negro race.

TABLE 2.—*Condition of Thyroid (White Race) Girls*

	Number	Per Cent
Examined	9,978	100
Normal 0	7,955	79.72
Group 1—Slight	1,717	17.21
Group 2—Moderate	254	2.55
Group 3—Marked	52	0.52
Groups 1, 2, 3—Total enlargements	2,023	20.28

This study was made only in the colored Manhattan group and by the same investigator who examined the white Manhattan group. Hence the incidence of thyroid enlargements among the Manhattan group of negro girls was only compared with the incidence of thyroid enlargements found among the Manhattan group of white girls.

TABLE 3.—*Condition of Thyroid in the White and in the Negro Race (Manhattan) (Girls)*

	White		Negro	
	Number	Per Cent	Number	Per Cent
Total examined (Manhattan)	5,119	100	1,106	100
Normal 0	4,305	84.1	956	86.4
Group 1—Slightly enlarged	690	13.5	129	11.57
Group 2—Moderately enlarged	103	2.0	17	1.54
Group 3—Markedly enlarged	21	0.4	4	0.36
Groups 1, 2, 3—Total enlargements	814	15.9	150	13.5

There seems to be no significant difference in the incidence (2.4 per cent) of thyroid enlargements between white and colored girls. The figures are slightly in favor of the colored girls. Age was not correlated in this comparison.

Group 1, consisting of slightly enlarged, often invisible, thyroid glands, is a somewhat debatable borderline group. The personal equation of the examiner is a greater factor in determining the size of this group than it is in the sizes of group 2 and 3. In my opinion, the group in its lower reaches contains subjects in whom the gland

varies little in size, if at all, from the standard accepted as normal, and the standard itself, it must be remembered, is not a scientific one, but is more or less arbitrary and debatable.

It will be remembered that Dr. Marine has stated that the thyroid requirement for the maintenance of a balance in the economy of the body for meeting the physiologic needs is not necessarily the same in any two persons. Thyroid enlargements ought to be expected, which are dependent on relative insufficiencies of iodine due to increased demands on the thyroid of a physiologic nature at puberty, and goiter at puberty is a "physiologic" work, or compensatory enlargement of the thyroid gland in response to a physiologic stimulus.

TABLE 4.—*Number and Percentage of Each Grade of Thyroid Enlargement by Age (White Girls) Manhattan and the Bronx*

Age	Number Examined	Normal*		Total Thyroid Enlargements		Slightly Enlarged		Moderately Enlarged		Markedly Enlarged		Combined Moderately and Markedly Enlarged	
		A	B	A	B	A	B	A	B	A	B	A	B
8	19	19	100	0	0	...	....	...	....	...	....	...	....
9	72	68	94.4	4	5.6	4	5.6	...	....	...	....	...	....
10	211	187	88.6	24	11.4	23	10.9	1	0.5	...	....	1	0.5
11	385	351	91.2	34	8.8	30	7.8	3	0.8	1	0.2	4	1.0
12	839	709	84.5	130	15.5	122	14.6	7	0.8	1	0.1	8	0.9
13	1,428	1,105	77.4	323	22.6	282	19.7	36	2.5	5	0.4	41	2.9
14	1,878	1,445	76.94	433	23.06	372	19.81	55	2.93	6	0.32	61	3.25
15	1,941	1,509	77.74	432	22.26	351	18.08	62	3.20	19	0.98	81	4.18
16	1,788	1,439	80.48	349	19.52	292	16.33	47	2.63	10	0.56	57	3.19
17	1,027	819	79.8	208	20.2	174	16.9	29	2.8	5	0.5	34	3.3
18	290	224	77.3	66	22.7	52	17.9	9	3.1	5	1.7	14	4.8
19	59	46	78.0	13	22.0	9	15.2	4	6.8	...	....	4	6.8
20	10	8	80.0	2	20.0	2	20.0	0	0.0	...	....	...	....
21	10	7	70.0	3	30.0	2	20.0	1	10.0	...	....	1	10.0
Not given	21	19	90.5	2	9.5	2	9.5	...	....	...	....	...	....
Totals	9,978	7,955	79.72	2,023	20.28	1,717	17.21	254	2.55	52	0.52	306	3.07

* A, number of normal or enlarged thyroids; B, percentage of normal or enlarged thyroids.

Many patients with simple goiter at puberty pass through the period of puberty and seem to be able to effect a spontaneous regression of the enlargement to the normal after the exciting cause is removed. This is common clinical observation. It is referred to by Marine [2] in his discussion of a survey of an older group of college women in the University of the State of Washington, in which he draws attention to the fact that the greatest incidence of thyroid enlargement occurs at puberty and that "a certain percentage of enlargements recede below the line of clinical perceptibility spontaneously"—and this in a goitrous region!

That there is in New York City a spontaneous regression of slight enlargements of the thyroid gland is indicated by the findings in table 4.

A study of these figures, which, of course, are only suggestive because of the small numbers examined, shows that the fourteenth year presents the highest percentage (23.06 per cent) of enlarged thyroids (table 4). The percentage incidence of enlarged glands increases

rapidly from the eleventh to the thirteenth year, when it remains almost constant to the fifteenth year when it decreases immediately. The figures between the eighteenth and the twenty-first year are not included, because the number of subjects examined in each of these years is too small to be looked on even as suggestive (chart 2, a).

The curve in chart 2, a, is suggestive of a spontaneous return toward the normal in a certain number of subjects at the sixteenth year. There were not a sufficient number of children examined above the age of 16 from which to determine accurately the direction of the curve after the sixteenth year.

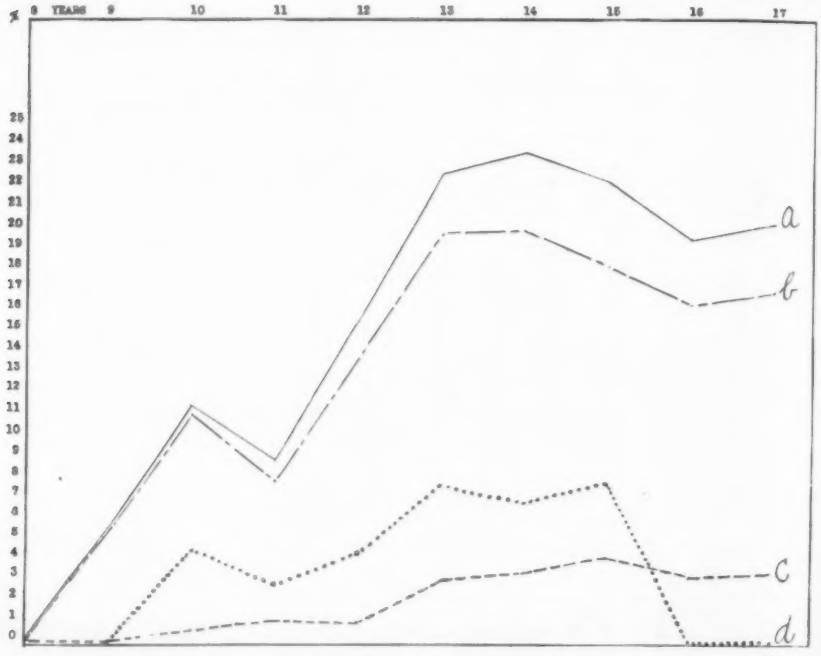


Chart 2.—Percentage incidence of enlarged thyroid glands in relation to age (girls and boys). (*a*) Girls (Manhattan and Bronx) total enlargements (groups 1-2-3). (*b*) Girls (Manhattan and Bronx) slight enlargements (group 1). (*c*) Girls (Manhattan and Bronx) moderate and marked (groups 2-3). (*d*) Boys (Manhattan) total enlargements (groups 1-2).

Furthermore, the figures in table 4 suggest that the highest incidence of slightly enlarged glands occurs in the thirteenth, (19.7 per cent), fourteenth (19.81 per cent), and fifteenth years (18.08 per cent), and is immediately followed by a distinct regression to 16.3 per cent in the sixteenth year. The figures between the years 18 and 21 are not included for the reason before stated (chart 2, b).

Again, combining the moderately and markedly enlarged groups (table 4), it will be seen that the greatest incidence of thyroid enlarge-

ment occurs in the fifteenth year (4.18 per cent), and is immediately followed by a recession to 3.19 per cent in the sixteenth year (chart 2, c). These figures suggest that the greater proportion of thyroid enlargements found in this survey may be intimately connected with the establishment of puberty.[13]

The suggestion, that the relative insufficiency of the thyroid gland at puberty shown by a slight compensatory enlargement of the gland may be self limited in a certain number of cases, seems to be further corroborated by the fact that the incidence of moderately and markedly enlarged glands is only 3.07 per cent in comparison with an incidence of 17.21 per cent of slightly enlarged glands. This point seems to be further confirmed by the fact that no markedly enlarged glands were observed before the eleventh year or after the eighteenth year.

The accuracy of these observations is corroborated by Horan's figures, which show an incidence of less than 3 per cent of enlarged thyroids among 7,500 women, between the ages of 20 and 30 years, examined by standards as precise as those used in this study.

This tendency to spontaneous regression of the thyroid gland after puberty is not so pronounced in endemic centers of goiter. In those centers the tendency is for the condition to persist and to progress insidiously to forms of greater severity.

These facts seem to indicate that while simple goiter in nongoitrous localities usually is a benign condition, in goitrous centers it may insidiously progress even to such conditions as cretininsm, mutism and idiocy.

THE THYROID GLAND AND THE MENSTRUAL FUNCTION

The survey of the girls included an attempt to correlate the thyroid condition with the menstrual function. This attempt is shown in table 5.

TABLE 5.—*Relation of Menstrual Cycle and Function of Thyroid Condition (White)*

	Total		1. Menstruation Present or Due in One Week		2. Never Menstruated		3. Not Given	
	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent
Total.....	9,978	.....	3,394	....	1,930	....	4,654	....
Normal.....	7,955	79.72	2,626	77.3	1,574	81.6	3,755	80.7
Enlarged.....	2,023	20.28	768	22.7	356	18.4	899	19.3

1. In the group which was menstruating or was due to menstruate within a week, at the time of the examination, 77.3 per cent show normal

13. Among the total cases of thyroid enlargement in Manhattan, there was only one patient with exophthalmic goiter, and she was a native of New York, and only one patient with simple goiter serious enough to require surgical treatment; she was a native and resident of Cleveland, Ohio.

thyroids as compared with 79.72 per cent, the percentage of normal thyroids in the entire group studied.

The figures show a decrease of the percentage of normality of the thyroid gland of 2.42 per cent during the active part of the menstrual cycle, and suggest that the percentage of normality in the thyroid varies inversely with the activity of the menstrual function.

2. In the group in which the menstrual function had not yet been established (girls who had never menstruated), 81.6 per cent evidenced normal thyroids as compared with 79.72 per cent of normal thyroids in the entire group, and with 77.3 per cent of normal thyroids in group 1, the group examined during the active phase of the menstrual cycle. These figures show an increase of percentage of normality of the thyroid gland of 1.88 per cent in a group who had never menstruated, over the percentage of normal thyroids in the entire group and of 4.3 per cent over the percentage of normality in group 1, the group examined during the active phase of the menstrual cycle.

3. The group, listed under the caption "not given," included a group of girls who, at the time of the examination were not menstruating nor due to menstruate within a week, but in whom the menstrual function had been established. In this group, 80.7 per cent showed thyroids of normal size as compared with 79.72 per cent, the percentage of normal thyroids in the entire group studied, and with 77.3 per cent of normal thyroids in group 1, the group examined during the active phase of the menstrual cycle. These figures show an increase of percentage of normality of the thyroid gland of 0.98 per cent in group 3, over the percentage of normal thyroids for the entire group, and of 3.4 over the percentage of normality in group 1.[14]

SUMMARY OF THE THREE GROUPS

This study suggests that the percentage of normal sized thyroids varies inversely with the activity of the menstrual function. Although not conclusive, it seems to support the observations of clinicians that in a certain number of cases the size of the thyroid glands varies with the different phases of the menstrual cycle, increasing during the active days of the cycle and decreasing during the rest period (chart 3).

THYROID SURVEY OF 783 SCHOOL BOYS IN MANHATTAN

This survey covered an examination of 783 boys from the fifth grade through the first year of high school.

---

14. In this survey, there were several patients who had not menstruated until the sixteenth and seventeenth years, and in most of these the thyroid glands were underdeveloped.

Table 6 shows that of 783 boys examined between the ages of 9 and 19 years, 741, or 94.6 per cent, had normal glands; 38, or 4.9 per cent, showed slight enlargements; and 4, or 0.5 per cent, showed moderate enlargements. There were no markedly enlarged glands among this group of boys.

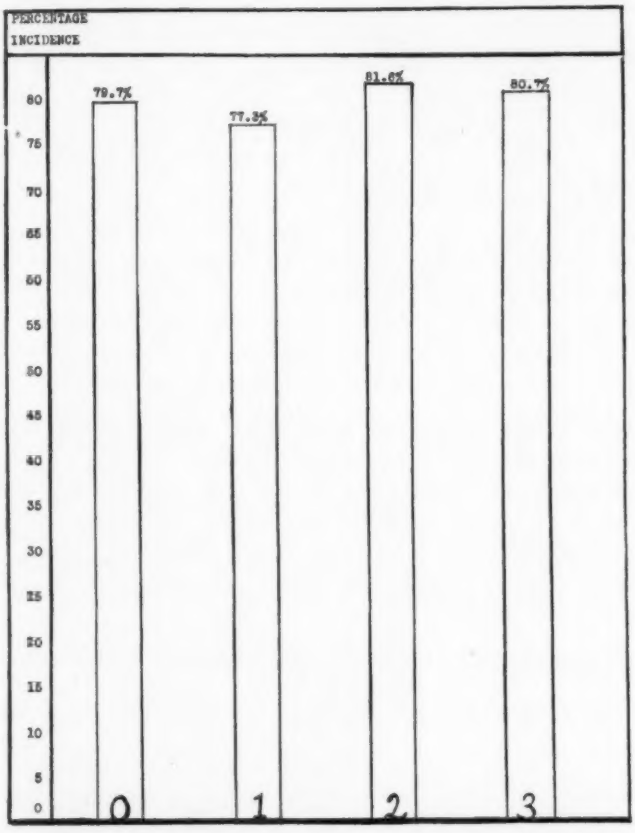


Chart 3.—Effect of the menstrual cycle and of the establishment of the menstrual function on the size of the thyroid gland (Manhattan and Bronx, girls, white). Percentage incidence of normal size thyroids: 0, in total group examined; 1, during active phase of menstrual cycle; 2, in group which had never menstruated; 3, during passive phase of menstrual cycle.

The table indicates that the greatest incidence of thyroid enlargements occurs at the establishment of puberty, from the thirteenth to the fifteenth years. The nineteenth year is not included because only two youths of this age were examined. The total number of boys examined is too small to give conclusive medical information, but the study suggests that among the boys of New York City the incidence of thyroid enlargement is small, the type mild, with a tendency to spon-

taneous regression after the fifteenth year, as there were no enlarged glands found after that year (chart 2, d), and as very few of the slightly enlarged glands tend to develop into moderate enlargements (table 6). The mild type is further indicated by the fact that there were no markedly enlarged glands among the group.

TABLE 6.—*Number and Percentage of Each Grade of Thyroid Enlargement (Boys) Manhattan*

Age	Number Examined	Normal		Slightly Enlarged		Moderately Enlarged		Total Enlargements	
		Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent
9	8	8	100	...	....	...	....	...	....
10	47	45	95.7	2	4.3	...	....	2	4.3
11	110	107	97.3	3	2.7	...	....	3	2.7
12	146	140	95.8	5	3.4	1	0.8	6	4.2
13	132	122	92.4	10	7.6	...	....	10	7.6
14	166	155	93.3	11	6.7	...	....	11	6.7
15	118	109	92.3	6	5.0	3	2.7	9	7.7
16	46	46	100.0	...	....	...	....	0	0.0
17	7	7	100.0	...	....	...	....	0	0.0
18	1	1	100.0	...	....	...	....	0	0.0
19	2	1	50.0	1	50.0	...	....	1	50.0
Totals	783	741	94.6	38	4.9	4	0.5	42	5.4

Table 7 indicates that, in New York City, thyroid enlargements occur less frequently in boys (5.4 per cent) than in girls (15.9 per cent), that is, at a rate of about 1 to 3. It will also be noted that the decrease in the rates for boys is particularly striking for moderately and markedly enlarged glands. The rate for slight enlargements among boys is nearly one-third the rate for girls, but the rate for moderate enlargements

TABLE 7.—*Comparative Thyroid Incidence Manhattan Group (White) Girls and Boys*

	Girls		Boys	
	Number	Per Cent	Number	Per Cent
Number examined	5,110	....	783	....
Normal	4,305	84.1	741	94.6
Slightly enlarged	690	13.5	38	4.8
Moderately enlarged	103	2.0	4	0.5
Markedly enlarged	21	0.4	0	0.0
Total enlargement	814	15.9	42	5.4

among boys is one-fourth the rate for girls, and the boys show no markedly enlarged glands while the girls show an incidence of 0.4 per cent of marked enlargements.

It was stated previously in this paper that the incidence of goiter in boys and men is an important index of the degree to which a definite region is goitrous.

The findings of this survey of 783 boys, in which precise standards were used, seem to indicate that New York City is not an endemic center of goiter.

CONCLUSIONS

The more important and suggestive points discussed in this study and disclosed by this survey of 11,084 school girls and 783 school boys in New York City are as follows:

1. The incidence of simple goiter in school children and in the older group of women, and the investigation into the conditions of iodine intake which determine endemic centers of goiter, do not justify a conclusion that New York City is an endemic center of goiter. The mild sporadic cases of simple goiter which occur among school children seem to be dependent on a relative insufficiency of iodine, due mainly to a physiologic cause, namely, puberty.

2. Thyroid enlargements occur in New York City about three times more frequently in girls than in boys.

3. Simple goiter among children in New York City reaches its peak at puberty, between the ages of 13 and 15, in both girls and boys.

4. The percentage of incidence of normal glands seems to vary inversely with the degree of activity of the menstrual cycle.

5. The mild cases of simple adolescent goiter observed among children in New York City seem to show, in the case of girls, a distinct tendency to spontaneous regression after puberty; in that of boys a complete regression.

RECOMMENDATIONS

The findings of this survey do not justify a recommendation for the adoption of a general municipal or school administered prophylaxis as a public health measure in New York City. Individual prophylaxis, the early recognition and cure by individual physicians and public health education in goiter prevention and cure, would seem adequate.[15]

To aid in the prevention and cure of simple goiter, it is suggested:

1. That physicians in "nongoitrous" centers be impressed with the importance of regarding simple goiter as a symptom of relative or absolute deficiency of iodine in the thyroid gland and of undertaking its prevention, early recognition and cure, especially during adolescence and pregnancy. That they consider the advisability of administering very small doses of iodine regularly to pregnant women, and thus possibly diminish the tendency to goiter at puberty.[16]

2. That the medical service, especially in high schools, but also in colleges, teachers' training schools and elementary schools, include an examination and notation of the condition of the thyroid gland. That

---

15. Marine, David, and Kimball, O. P.: The Prevention of Simple Goiter in Man, Arch. Int. Med. **25**:661-692 (June) 1920.

16. Kimball, O. P.: The Prevention of Simple Goiter in Man, Am. J. M. Sc. **163**:634 (May) 1922. Marine, David: The Prevention of Goiter, J. Pub. Health, Mich. **11**:23-24, 1923.

cases of thyroid enlargement be reported to parents, with instructions to seek medical advice.

3. That parents be informed that simple goiter can be prevented and cured, especially in the early stages of development, by minute doses of iodine; that they be impressed with the importance of preventing and curing simple goiter, especially during adolescence and pregnancy, and that they be encouraged to seek periodically medical advice for their children and for themselves.

4. That the cooperation of the medical profession be enlisted through appropriate channels, the boards of health, the academies of medicine, etc., and that public health information be given on the method of goiter prevention and cure.

5. That the hygiene of all girls at puberty be supervised with great care as to rest and diet, and freedom from nervous excitement and fatigue. Instruction should be given in the need of iodine-containing foods—sea foods, especially.

6. That because of the comparatively small incidence of simple adolescent goiter in New York City, its mild type and its tendency to regress spontaneously after puberty, great care should be taken not to alarm the public by unduly or unwisely stressing the conditions.

7. That other Atlantic sea coast cities, such as Portland, Baltimore, Charleston and New Orleans, publish goiter statistics indicating the incidence and type of goiter among different units of the population.

609 West 114th Street.
1925.

THE KIDNEY: A FILTER FOR BACTERIA

VI. THE EFFECT OF URETERAL OBSTRUCTION ON THE EXCRETION OF BACTERIA *

HENRY F. HELMHOLZ, M.D.
AND
RUTH S. FIELD, B.A.
Laboratory Assistant
ROCHESTER, MINN.

Perhaps the best mode of studying the density of the kidney filter for a short time is to produce a hydronephrotic sac by tying the ureter. In this way, all the bacteria that are excreted during a short period can be retained. For longer periods of time this would not necessarily hold true, as bacteria are rapidly absorbed from a closed sac and can be early demonstrated in the circulation, as shown by Magoun [1] and others. If no growth of bacteria in such a closed sac occurred, it is conceivable that there might be partial sterilization by the production of a hydronephrotic sac.

If it is true, as maintained by Biedl and Kraus,[2] Rolly,[3] David and McGill,[4] and others, that bacteria are being excreted by the kidney in large number during the first hours after intravenous injection, then surely they should be constantly present in hydronephrotic sacs. If bacteria are not found in the sacs and it can be shown that the urine in early hydronephrotic sacs is not bactericidal, then it must logically follow that under these conditions bacteria are held back by the kidney in spite of the slight injury that the back pressure may have produced. It would seem, therefore, that negative results from this series of experiments would be crucial in deciding the question of the constant and rapid excretion of bacteria by the kidney.

TECHNIC

The abdomen of the animal was opened under ether anesthesia. In one series of experiments the ureter was clamped for varying periods up to four hours, then released, just before the intravenous injection

* Received for publication, Feb. 11, 1926.

* From the Section on Pediatrics, Mayo Clinic.

1. Magoun, J. A. H.: Pelvis of Kidney as Possible Source of Infection of Blood Stream, J. A. M. A. **74**:73-75 (Jan. 10) 1920.

2. Biedl, Arthur, and Kraus, Rudolf: Ueber die Ausscheidung der Mikroorganismen durch die Niere, Arch. f. exper. Path. u. Pharmakol. **37**:1-25, 1896.

3. Rolly, F.: Zur Frage der Durchgängigkeit der Niere für Bacterien. München. med. Wchnschr. **56**:1873-1875, 1909.

4. David, V. C., and McGill, E. C.: The Relation of the Bowel to B. Coli Kidney Infections, J. Urol. **10**:223-254, 1923.

of the bacteria. In the second series of experiments, the ureter was tied at about the middle point and the bacteria injected. In a certain number of experiments in both series, at or shortly before the intravenous injection of the organism, 20 per cent sucrose was given intravenously in order to increase the excretion of urine and to intensify the hydronephrosis. At the end of the determined interval, the animal was chloroformed and the kidney removed from the abdominal cavity, the ureter being cut well below where it was tied, and specimens of urine readily obtained from the hydronephrotic sac. The ureter was seared just above the ligature and a capillary pipet was introduced; sufficient urine was obtained to make both brain-broth and litmus-lactose-agar cultures. In all of the experiments in which the hydronephrosis lasted longer than two hours, blood was found in the collected urine. It could usually be seen macroscopically, but was always to be demonstrated

TABLE 1.—*The Effect of Temporary Clamping of Ureter on Excretion of Staphylococcus*

Number	Minutes After Release of Ureter From Time of Injection to End of Experiment	Minutes Ureter Was Clamped	20 per Cent Sucrose Injected, Cc.	Bladder Urine Culture	Remarks
744	85	15	300	0	Blood 1 in urine
745	175	15	200	0	Blood 1 in urine
746	180	60	320	0	
747	180	60	560	0	
748	180	240	360	0	
749	105	240	150	0	
750	180	240	200	+	Blood 4 in urine
751	180	240	350	0	
768	12	240	25	0	
769	120	240	125	0	
757	230	240	0	0	
758	210	240	0	+	Blood clots
759	195	240	0	0	Blood 4 in urine
760	195	240	0	0	Blood 4 in urine

microscopically. All cultures were incubated for forty-eight hours. Aseptic technic was used in all operations when the experiments were to last longer than seven hours. Two cubic centimeters of a twenty-four hour culture of bacteria was injected in all experiments.

THE EFFECT OF TEMPORARY CLAMPING OF THE URETER ON THE PASSAGE OF STAPHYLOCOCCUS THROUGH THE KIDNEY

This series of experiments was done to see whether, after temporarily clamping the ureter, changes would be produced in the kidney that would allow bacteria to pass through (table 1). In two rabbits the ureter was clamped for fifteen minutes; the clamp was removed, 2 cc. of a twenty-four hour culture of staphylococcus was given, followed by a 20 per cent sucrose solution intravenously to produce diuresis. Eighty-five, and one hundred seventy-five minutes after the intravenous injection of the staphylococcus the animals were killed; no bacteria appeared in

the urine. Two similar experiments were done in which the ureters were clamped for sixty minutes, the animals being killed three hours after the injection of staphylococcus; cultures of the urine were negative. In six experiments, the ureters were clamped for four hours and the animals were killed by chloroform twelve minutes, one hundred and five minutes, and two and three hours, respectively, after the injection of bacteria. Although the six urine specimens contained much blood, bacteria were grown in only one of the six cultures.

For comparison with the series of experiments in which diuresis was produced by sucrose, four animals were injected with bacteria and allowed to live for, respectively, one hundred and seventy-five, one hundred and ninety-five, two hundred and ten, and two hundred and thirty minutes after injection, without producing diuresis. The urine of three of these four animals contained blood, but bacteria were cultured from the urine in only one of them. It is striking that the cultures were not positive in all the urine in which blood was found. To determine the possible bactericidal action of the urine containing blood from a hydronephrotic kidney, six different specimens were inoculated with the same organisms used in these experiments and the urine plated at the end of one hour, and of eighteen hours. In every instance the organisms grew luxuriantly.

Typical Experiments (Series 1).—Rabbit 748: A rabbit, weighing 1.75 Kg., was etherized and the right ureter tied and the left ureter clamped for four hours. There was marked distension of the left ureter above the clamp. The ureter remained compressed, although it seemed to be functioning at the end of the experiment. After removing the clamp, intravenous injection of 10 per cent sucrose was begun. Two cubic centimeters of a salt suspension of a twenty-four hour dextrose brain-broth culture of virulent staphylococcus was injected. Three hours later the rabbit was killed. Three hundred and sixty cubic centimeters of sucrose had been given and 275 cc. of urine had been passed; none had been passed during the period of clamping. At necropsy, 25 cc. of urine was found in the bladder. This urine cultured in litmus lactose agar was negative; the microscopic examination showed ten red blood cells to one low power field magnification. Caudate epithelium was present and the urine was positive for sugar. The blood culture showed staphylococcus.

Rabbit 750: A rabbit, weighing 1.5 Kg., was etherized; the right ureter was tied and the left ureter was clamped for four hours, at the end of which period both kidneys appeared normal. Intravenous injection of 10 per cent sucrose was begun and 2 cc. of salt suspension of a twenty-four hour dextrose-brain-broth culture of a virulent staphylococcus was injected. Three hours later, the rabbit was killed. The

bladder contained 20 cc. of urine. Two hundred cubic centimeters of sucrose had been given and 175 cc. of urine had been passed. Urine from the right ureter was sterile. Both litmus-lactose-agar plates of urine from the bladder showed 20 colonies. There was sugar and red blood cells (4) in the urine.

Rabbit 758: A rabbit, weighing 1.25 Kg., was etherized, and the right ureter tied and the left clamped for four hours. After removal of the clamp, 2 cc. of salt suspension of a twenty-four hour dextrose-brain-broth culture of a virulent staphylococcus was injected intravenously. The rabbit was killed three and a half hours later. No urine was passed during the experiment. The bladder urine was filled with blood clots, and when cultured in litmus lactose agar, showed innumerable colonies of staphylococci. Litmus-lactose-agar cultures from the urine of the right ureter were negative.

THE EFFECT ON THE PASSAGE OF BACTERIA OF TYING THE URETER THROUGH THE KIDNEY

In this series of thirty-five experiments, the time between the injection of bacteria into the vein and the death of the animals ranged from twelve minutes to three hours, and the duration of the hydronephrosis from twenty minutes to seven hours. The hydronephrosis always covered the whole period from the injection of the organism to the death of the animal. The colon bacillus and the staphylococcus were the organisms used. Every effort was made, by using large quantities of sucrose, to obtain extreme hydronephrosis in less than two hours. Although blood was found regularly in the urine when the ureter was tied for longer periods, bacteria could be cultivated from the urine in only two instances, after two hours of hydronephrosis and two-hour intervals between injecting and killing the animal. The surprising fact is not that bacteria appeared on culture in these two specimens of urine, but that bacteria were absent in the other nine specimens which showed large amounts of blood. In forty-nine experiments in these two series, including all cases of clamped or ligated ureters, we found bacteria in the urine from the hydronephrotic kidney in only four instances.

Typical Experiments (Series 2).—Rabbit 736: A rabbit, weighing 1.6 Kg., was etherized, the right and left ureters were tied and an intravenous injection of 130 cc. of 20 per cent sucrose was given. Two cubic centimeters of a salt suspension of a twenty-four-hour dextrose-brain-broth culture of a virulent staphylococcus was injected into the marginal ear vein. Two hours later the rabbit died. The urine in the ureters was filled with red blood cells, and when cultured in litmus lactose agar showed staphylococci.

Rabbit 739: A rabbit, weighing 1.35 Kg., was etherized and the right and left ureters were tied. Two cubic centimeters of a salt suspension of a twenty-four-hour culture of virulent staphylococcus, and 110 cc. of 20 per cent sucrose, were injected intravenously. Two hours later the rabbit was killed. The bladder urine was cultured in litmus lactose agar; one plate was negative, the other showed six colonies of staphylococcus. Culture of urine from the right ureter in dextrose brain-broth was negative; urine from the left ureter in litmus lactose

TABLE 2.—*The Effect on the Passage of Bacteria of Tying the Ureter through the Kidney When Aided by Sucrose Diuresis*

Rabbit	Organism	Minutes of Hydronephrosis	Minutes from Injection of Organism to Death	Blood in Ureteral Urine	Bacteria in Urine from Hydronephrotic Sac
768	Staphylococcus	242	12	0	0
727	Staphylococcus	145	25	0	0
720	Staphylococcus	60	30	0	0
723	Staphylococcus	90	30	0	0
722	Staphylococcus	100	40	0	0
729	Staphylococcus	170	50	0	0
728	Staphylococcus	180	60	0	0
741	Staphylococcus	70	70	0	0
742	Staphylococcus	85	85	0	0
744	Staphylococcus	100	85	0	0
724	Staphylococcus	215	95	0	0
740	Staphylococcus	105	105	0	0
749	Staphylococcus	345	105	0	0
739	Staphylococcus	120	120	+	+
738	Staphylococcus	120	120	+	0
736	Staphylococcus	120	120	+	+*
769	Staphylococcus	360	120	—	0
719	Staphylococcus	165	135	—	0
745	Staphylococcus	190	175	+	0
743	Staphylococcus	180	180	+	0
746	Staphylococcus	240	180	+	0
747	Staphylococcus	240	180	+	0
748	Staphylococcus	420	180	+	0
750	Staphylococcus	420	180	+	0
751	Staphylococcus	420	180	+	0
683	Bacillus coli	20	17	0	0
684	Bacillus coli	32	32	0	0
695	Bacillus coli	43	40	0	0
685	Bacillus coli	60	60	0	0
687	Bacillus coli	60	60	0	0
732	Bacillus coli	120	60	0	0
735	Bacillus coli	105	75	0	0
734	Bacillus coli	150	90	0	0
731	Bacillus coli	150	90	0	0
733	Bacillus coli	185	125	+	0

* Animal died.

agar showed staphylococci. The urine from both ureters contained red blood cells. This and the preceding case comprise the only two in the series in which the urine gave a positive culture.

THE LENGTH OF TIME NECESSARY FOR INTRAVENOUSLY INJECTED BACTERIA TO APPEAR IN THE HYDRONEPHROTIC SAC

Having determined in the previous experiments that bacteria do not appear in a hydronephrotic sac in the course of three hours, an attempt was made to learn whether bacteria would appear in the urine from a hydronephrotic sac earlier than in the urine from a kidney not

obstructed. Organisms of known virulence such as the staphylococcus, which previous experiments had shown would pass through the uninjured kidney in seven hours, and also avirulent staphylococci, virulent and avirulent colon bacilli, and *Streptococcus lacticus,* were used.

Two of the six animals receiving virulent staphylococci were killed after five hours, two after six hours, and two after seven hours. In the two five-hour experiments, the urine from the left hydronephrotic sacs was negative on culture, and the urine from the right hydronephrotic

TABLE 3.—*The Appearance of Bacteria in the Urine from Hydronephrotic Sacs After Intravenous Injection*

Rabbit	Organism	Hours from Injection to Death	Urine Culture, Left Hydronephrotic Sac		Urine Culture, Right Hydronephrotic Sac		Blood Culture	Remarks
			DBB	LLA	DDB	LLA		
980	Virulent Bacillus coli.....	2	0	0	0	0	+	
981	Virulent Bacillus coli.....	2	+	+	0	0	+	Streptococcus, gram negative bacillus, Bacillus coli; probably contamination
977	Virulent Bacillus coli.....	3	0	0	0	0	+	
978	Virulent Bacillus coli.....	3	0	0	0	0	+	
979	Virulent Bacillus coli.....	3	0	0	0	0	+	
962	Virulent Bacillus coli.....	4	+	+	+	+	+	
952	Virulent Bacillus coli.....	5	+	+	+	+	+	
953	Virulent Bacillus coli.....	5	0	0	0	0	+	
956	Virulent Bacillus coli.....	6	+	+	+	+	+	
957	Virulent Bacillus coli.....	6	+	+	+	+	+	
954	Virulent Bacillus coli.....	7	+	+	+	+	+	
955	Virulent Bacillus coli.....	7	+	+	+	+	+	
963	Virulent Bacillus coli.....	24	+	+	+	+	+	
976	Avirulent Bacillus coli.....	24	+	+	+	+	+	
992	Avirulent Bacillus coli.....	24	+	+	+	+	+	
965	Avirulent Bacillus coli.....	24	0	0	+	+	+	
948	Virulent staphylococcus...	5	0	0	+	+	+	Four colonies
949	Virulent staphylococcus...	5	0	0	+	+	+	Eighteen colonies
946	Virulent staphylococcus...	6	0	0	0	0	0	
947	Virulent staphylococcus...	6	0	0	0	0	0	
950	Virulent staphylococcus...	7	0	0	0	0	+	
951	Virulent staphylococcus...	7	+	+	0	0	+	
960	Avirulent staphylococcus..	6	—	0	+	0	+	
961	Avirulent staphylococcus..	6	—	+	—	+	+	
958	Avirulent staphylococcus..	7	0	0	0	0	+	
957	Avirulent staphylococcus..	7	—	0	+	+	+	
974	Avirulent staphylococcus..	24	0	0	0*	0	+	
975	Avirulent staphylococcus..	24	+	+	0*	0	+	
991	Avirulent staphylococcus..	24	+	+	+*	+	+	
964	Avirulent staphylococcus..	24	+	+	0*	0	+	
982	Streptococcus lacticus.....	24	0	0	0*	0	0	
983	Streptococcus lacticus.....	24	0	0	0*	0	0	

Both ureters tied and rabbits injected intravenously. Macroscopic blood in the urine from each hydronephrotic sac.
* Bladder cultures. Right ureter not tied.

sacs was positive in each instance. In one specimen there were four colonies on the plate; in the other eighteen. In the two six-hour experiments, organisms were not found on culture from either the right or the left kidney. In the entire series of experiments, the blood cultures from these two rabbits were the only negative cultures, except those in the experiments in which the *Streptococcus lacticus* was used. It is difficult to explain the failure of growth of the organism, as in other animals injected with the same cultures the cultures of the urine and

blood were positive. In one seven-hour experiment the urine from both sacs was negative; in the other experiment the urine from one kidney was sterile and from the other was positive for bacteria.

The avirulent staphylococcus was injected into eight animals, two of which were killed after six hours, two after seven hours, and four after twenty-four hours. The two six-hour experiments showed in one instance positive findings in the urine from both kidneys; in the other instance the findings were negative from the left, and positive from the right kidney. The findings in the urine in one seven-hour experiment were negative from both kidneys, and in the other experiment they were negative from the left, and positive from the right kidney. In the twenty-four-hour experiments only the left ureter was tied. One twenty-four-hour experiment gave negative findings in the urine from the hydronephrotic sac and from the bladder. In the other three experiments, the urine from the right kidney was sterile, but in all three specimens of urine from the hydronephrotic kidney there was growth of bacteria.

Thirteen experiments were carried out with virulent colon bacilli; two animals were killed two hours after the injection of the organisms, three after three hours, one after four hours, two after five hours, two after six hours, two after seven hours, and one after twenty-four hours. The blood cultures were all positive. The findings in the urine from the hydronephrotic sac were positive (with one exception) in all experiments that ran four hours or longer. One four-hour experiment disclosed sterile urine from both sides. In one two-hour experiment, the urine from the left kidney contained bacteria, but as these were streptococci and a large gram-negative bacillus besides the colon bacillus, it seemed probable that this urine was contaminated while the cultures were being taken. The three three-hour experiments were negative.

Only three experiments, all twenty-four hours long, were done with the avirulent colon bacilli. Two of these were positive for bacteria in the urine from both kidneys, and the third showed growth in the urine from one kidney but not from the other.

No bacteria were found in the urine from both kidneys in the two twenty-four-hour experiments in which *Streptococcus lacticus* was injected intravenously.

The pathologic anatomy of this series of experiments has no direct bearing on the problem in hand and consequently will not be discussed here, but will be taken up as a separate study on the differential lesions of hydronephrotic sacs infected from the blood stream and by the ascending route.

From the urine of a patient dying from pyelitis, we isolated *Streptococcus fæcalis*, that, when injected intravenously into rabbits, appeared

in the urine with some regularity after twenty-four hours, but in no instance were we able to show that there was any pus in the urine The organism seemed, therefore, to be a good one to test out for its ability to penetrate the renal filter when influenced by hydronephrosis. A series of thirteen experiments was done in which both ureters were tied and the animals were killed from one to eight hours after the intravenous injection of the organism (table 4). After one hour, no organisms were grown from the ureteral urine from either kidney. The amounts of urine obtainable were very small, and in one instance none was secured from the left kidney. Only culture on litmus agar was done. In the two experiments that lasted one and a half hours, the culture from the right kidney in one case showed a single colony; the other three cultures were sterile. The three experiments that lasted for two hours showed a single colony on the litmus-lactose-agar plate

TABLE 4.—*Appearance of Streptococcus Fæcalis in the Urine of a Hydronephrotic Sac After Intravenous Injection*

Rabbit	Hours from Intravenous Injection to Death of Animal	Culture of Urine from Hydronephrotic Sacs				Remarks
		Right		Left		
		Brain Broth	Litmus Agar	Brain Broth	Litmus Agar	
331	1	..	0	..	0	Insufficient urine for all cultur
272	1	.	0	..	—	No urine obtainable from left
239	1½	..	+*	..	0	
340	1½	..	0	..	0	
341	2	0	+*	0	0	
342	2	0	0	0	0	
113	2	0	0	0	0	
114	4	0	0	0	0	
115	4	..	0	0	0	
116	4	+	+	0	0	
117	4	+	..	0	0	
118	7	+	0	+	+	
119	8	+	..	+	..	

* One colony.

of the urine from the right kidney. The brain-broth culture from the same urine was negative. The other five specimens were negative on culture both in brain broth and litmus lactose agar. The four-hour experiments showed two with sterile urine from both kidneys and two with sterile urine from the left ureter and urine containing bacteria from the right ureter. The urine in the seven and eight-hour experiments was positive for bacteria from both ureters.

COMMENT

The outstanding feature of these experiments is the ability of the kidney to maintain the bacterial filter for a number of hours with a blocked ureter; of almost equal interest is the frequency with which blood was found in the urine from the hydronephrotic sac, and the relative infrequency with which bacteria could be grown from such speci-

mens. We felt that in using the colon bacillus and the staphylococcus, growth would take place even if there were only very few organisms present, and that if these organisms did not grow others would not be likely to do so.

In twenty-three experiments of less than one and a half hours, we never obtained a growth of bacteria from the urine even with maximal diuresis. This result, we believe, is of great importance in showing that the rapid excretion of bacteria through the kidney, as apparently demonstrated by various authors, does not take place. Even under these unfavorable conditions, the kidney does not allow bacteria to pass during an interval of less than one hour and a half when practically all the urine in the hydronephrotic sac is cultured.

From the summary of the experiments (table 5), it is seen that in twenty-three experiments in which the duration of the experiment was less than one and one-half hours, bacteria were never grown from the urine of the hydronephrotic sac. When the time interval between the intravenous injection and the death of the animal was from one and a

TABLE 5.—*Summary of Experiments*

Number of Experiments	Time Interval	Bacteria in Urine from Hydronephrotic Sac	Sterile Urine from Hydronephrotic Sac
23.....	Up to 1½ hours	0	23
20.....	1½ to 2 hours	5*	15
16.....	2 to 3 hours	1	16
5.....	3 to 4 hours	3	2
10.....	4 to 6 hours	7	3

* One definitely contaminated. Two showed only 1 colony on plate.

half to two hours, fifteen experiments showed sterile urine and five showed growth of bacteria. Of these five, one specimen was definitely contaminated and in two others there was but a single colony on the plate. The other two contained large numbers of organisms. Of the sixteen experiments in which the time interval was from two to three hours, fifteen showed sterile urine and one showed bacteria on culture of the urine. In the three- to four-hour group, three were positive and two negative, while in the four- to six-hour group, seven were positive and three negative.

The series shows very definitely that for the shorter intervals the urine secreted within the hydronephrotic sac is sterile. In the experiments with the increasing time intervals up to seven hours, over two-thirds of the urine specimens were positive. In the twenty-four-hour experiments with *Streptococcus lacticus* and avirulent staphylococcus, sterile urine was found in the hydronephrotic sacs, although in no instance was the urine sterile with the avirulent colon bacillus.

There were red blood cells in practically all the specimens of urine from which bacteria were cultured. When the hydronephrosis lasted

longer than three hours, the urine invariably contained red blood cells in large numbers. To determine the possible bactericidal power of the rabbits' urine, organisms were grown in the urine from the hydronephrotic sac, obtained with and without diuresis. As a further control, a certain number of organisms were injected into the pelvis, and the ureter was tied and allowed to remain thus for four hours. At the end of this period the urine was measured, cultured, and the number of bacteria found were compared with the number of bacteria injected. No bactericidal effect was noted.

Virulent colon bacilli appeared earlier in the urine than virulent staphylococci. The colon bacilli appeared after four hours and regularly after six. The staphylococci appeared in the urine from one kidney in two five-hour experiments, but not in two after six hours, and in only one of two seven-hour experiments. In the four twenty-four-hour experiments with colon bacilli, all the specimens were positive except the urine from the left kidney in one of the experiments in which avirulent colon bacilli were used. In one of four experiments with avirulent staphylococci, the urine from both kidneys was sterile, and in two experiments the urine from one kidney was sterile, making just one-half sterile and one-half not sterile. The two twenty-four-hour experiments in which *Streptococcus lacticus* was used were both negative for bacteria.

These results, we believe, are of the utmost significance in deciding the question of the excretion of bacteria by the kidney. If, as is stated by Biedl and Kraus and others, bacteria pass out into the urine constantly in one hour or less, then bacteria should have been found constantly in the hydronephrotic sacs, but instead, they were never found in twenty-three experiments in which the animals were allowed to live less than one hour and a half after intravenous injection, and only six times in thirty-six experiments that lasted from one and a half to three hours. Of equal importance are the twenty-four-hour experiments which show sterile hydronephrotic sacs after the intravenous injection of avirulent staphylococcus, and *Streptococcus lacticus*. Not only do these twenty-four-hour experiments show that the kidney does not secrete bacteria, but that it has the ability to hold back organisms that are circulating through it when definitely injured by the pressure of hydronephrosis. It is of interest, furthermore, that constantly after twenty-four hours, large numbers of pus cells are found in the urine. This led us to think that there must be an infection present until we repeated the experiment without bacterial injection, and found that large numbers of pus cells were constantly present in the urine after twenty-four hours in a sterile hydronephrotic sac.[5]

5. Helmholz, H. F.: Acute Changes in the Kidney and Pelvis Produced in the Rabbit by Tying the Ureter. (To be published.)

SUMMARY

The kidney of a normal rabbit constantly holds back bacteria, intravenously injected, from entering the urine of a hydronephrotic sac for periods up to one and a half hours. Only exceptionally are bacteria found until after three hours have elapsed. With marked diuresis, bacteria appeared in the hydronephrotic sac as early as two hours after injection. Avirulent organisms are held back longer than virulent organisms, even for periods of twenty-four hours. After three hours, blood appeared regularly in the urine from the hydronephrotic sac.

PROGRESS IN PEDIATRICS

FLATFOOT IN INFANTS AND IN CHILDREN*

PHILIP LEWIN, M.D.
Assistant Professor of Orthopedic Surgery, Northwestern University Medical School; Attending Orthopedic Surgeon St. Luke's and Cook County Hospitals
CHICAGO

The subject of flatfoot among infants and children is becoming more and more important. The condition has not been given proper consideration by the majority of pediatricians. Concerning the etiology of flatfoot, heredity is undoubtedly a very important factor, and in my experience the paternal parent is usually the one involved. The age varies from birth to adolescence. The various periods at which feet should be inspected are: at birth, 6 months, 1 year, 2 years, 3 years, 4 years and at adolescence. There is no difference between the frequency of occurrence in the two sexes, although it appears to predominate slightly in males. Naturally, one would anticipate more anatomic deviation in the negro, but it does not follow that the disability or discomfort is more common in that race. Some disturbance in intra-uterine life might explain some cases, namely: anomalies of the amnion, or unusual foot position. In amyotonia congenita of Oppenheim, flatfoot or "pad foot" is the rule. The same condition is often seen in cases of pseudohypertrophic muscular paralysis before equinus develops. Any condition causing weakened musculature may cause flatfoot. I have had one case following diphtheria; a typical postdiphtheric peripheral neuritis.

There is a definite type of weak, pronated or flatfoot that appears coincident with adolescence, in long slender rapidly growing feet, especially in girls. Focal infection such as tonsillitis or any infectious disease causes flatfoot by a toxic relaxation of the supporting structures, unprotected by proper prophylactic measures to be discussed under treatment. These infections might cause a toxic arthritis, with resulting rigid valgus deformity which is quite resistant to treatment.

Obesity causes flatfoot in two ways: first, by the strain of an excessive load when there is usually a disproportion between the weight to be carried and the size and power of the feet and lower legs; second, by the glandular disbalance, which is found in conditions such as dystrophia

* Received for publication, April 7, 1926.
* Read by invitation before the Chicago Pediatric Society, Jan. 19, 1926.

adiposogenitalis of Froehlich, in which, usually associated with talipes valgus, there is genu valgum due to relaxation of the supporting structures of the inner border of the knee.

Trauma may result in a pronated foot. Infantile paralysis is a frequent cause of valgus deformity. The pathology is practically entirely pathologic anatomy, and is concerned with the mechanical effects on muscles, ligaments, and capsules of the joints and bones. In order to clarify the subject, a short discourse on the terminology, physiology and anatomy is given.

TERMINOLOGY

The generic term for foot deformities is "talipes," derived from talus (astragalus) and pes (foot). If the toes are at a lower level than the heel, the term equinus is used; if the heel is lower than the toes, the term calcaneus is used. In addition to either of these positions, if the foot is rotated on the long axis of the leg, the terms varus and valgus are used.

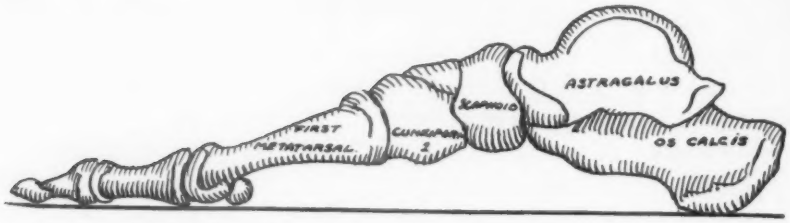
Inversion	Adduction	Supination	Varus
Eversion	Abduction	Pronation	Valgus

Talipes { *Equino* { *Varus* / *Valgus* } / *Calcaneo* { *Varus* / *Valgus* } }

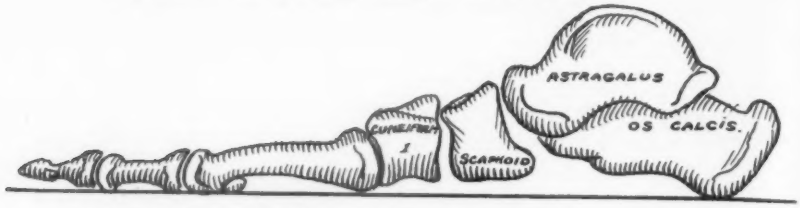
Inversion of the foot means simply elevating the outer border. When a foot is inverted, there is a tendency for the fore part of the foot to approach the midline of the body, that is, adduction. This movement occurs chiefly at the tarsometatarsal articulations. With eversion, there is a strong inclination to the opposite movement at these joints, namely, abduction. When a foot is inverted and adducted, there is usually an upward and outward rotation of the medial bones of the midtarsal region, namely, the scaphoid, first and second cuneiform bones. This constitutes supination. If a foot is everted and abducted, the reverse occurs, that is, downward and inward rotation of the medial midtarsal bones producing pronation. A foot that is inverted, adducted and supinated is said to be in varus position, and a foot that is everted, abducted, and pronated is said to be in valgus position. The following diagrams will be found useful in mentally fixing these terms.

PHYSIOLOGY

The physiology of the foot consists chiefly of the mechanics of a member whose function is twofold; first, weight bearing and second, flexible locomotion.

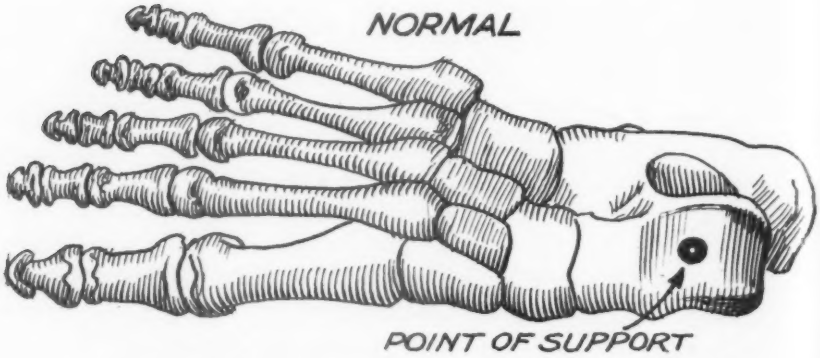


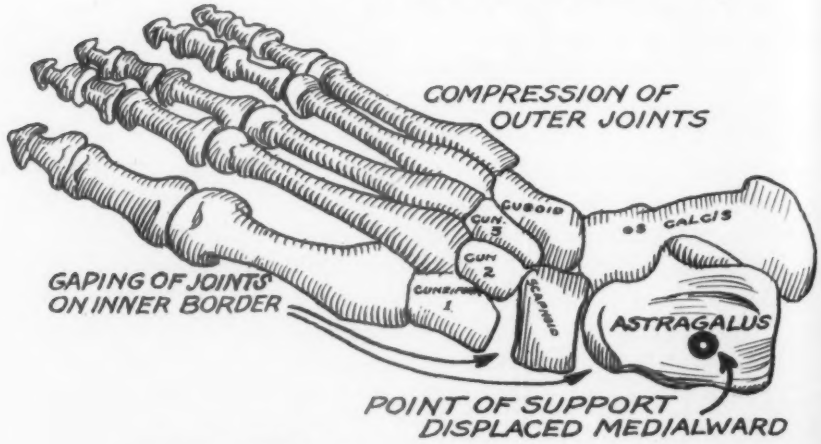
NORMAL INNER SIDE OF FOOT



FLAT FOOT INNER VIEW
SHOWING DEPRESSED ARCH
AND JOINT SEPARATION.

Fig. 1.—Normal and flatfoot.





FLAT FOOT

Fig. 2.—Normal and flatfoot.

Weight Bearing Line.—Normally, a plumb line dropped from the middle of the patella falls through the middle of the astragalus, and a point between the bases of the first and second toes. In a normal foot, a line drawn through the middle of the great toe and continued backward passes through a central point in the heel, and is known as Meyer's line.

Two bones of great importance are the astragalus and os calcis; the former because it is the mortise bone between the leg and the foot. The astragalus articulates with the tibia, fibula, scaphoid, and with the

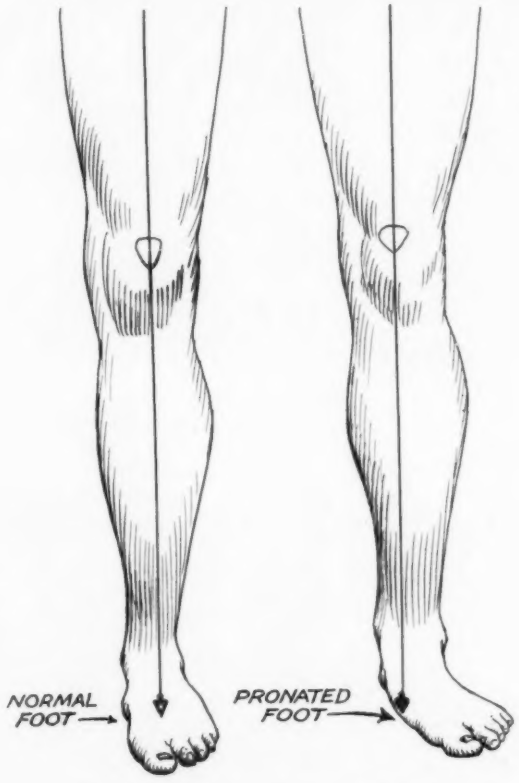


Fig. 3.—Normal and Pronated foot.

os calcis in three places; it cannot move itself because it has no muscle attachments; it is subjected to more superincumbent weight than any other bone in the body. The os calcis is important because of its attachment for the Achilles tendon and plantar fascia, and furnishing the initial bearing surface of the foot as it strikes the ground in walking. The scaphoid and first cuneiform bones owe their importance to the attachments of ligaments, and especially the tendons of the peroneus longus, and anterior and posterior tibial muscles.

The longitudinal arch is composed of the os calcis, astragalus, scaphoid, first and second cuneiforms, the first metatarsal and the phalanges of the great toe. When a foot is in action it is supported chiefly by muscles, but when standing, chiefly by ligaments.

ANATOMY

The pathologic anatomy of pronated feet consists of inward rotation of the superior portion of the os calcis. Insertion of the Achilles tendon is lateral. It is difficult to say whether this is cause or effect.

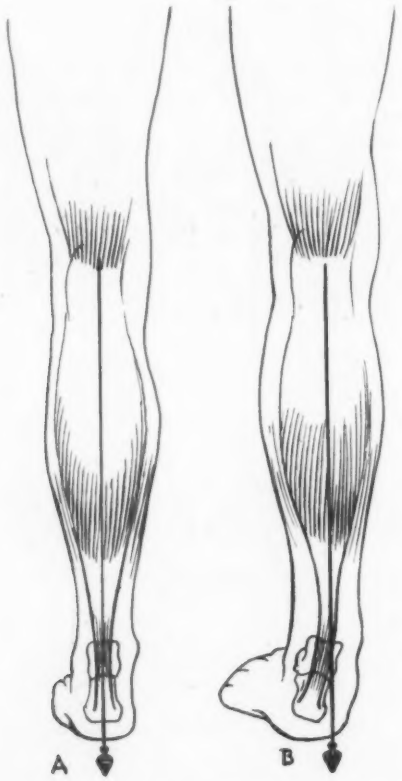


Fig. 4.—A, normal foot; B, foot showing Helbing sign, which illustrates the curve of the Achilles tendon.

The upper border of the astragalus is tilted mediad, carrying the inner border lower than the outer so that the weight strikes a glancing instead of a square blow. Mechanically, this is poor. The peroneal tendons are contracted because they are allowed to shorten. The anterior and posterior tibial tendons are stretched and lose their power. It is a physiologic law that when a normal tendon is overstretched it loses power, and when allowed to shorten it usually contracts and gains in

strength. This law applies equally to the capsules of the joints and the ligaments. The external lateral ligament and the external portion of the capsule of the joint are shortened and contracted. The internal lateral ligament and the internal portion of the capsule are stretched and weakened. The deltoid ligament is stretched, as are the ligaments

Fig. 5.—A, flatfoot in a boy, aged 14 years B, same a, A, showing a positive Helbing sign; C, the same boy, performing exercise 2. Note the prominent tibial tendons.

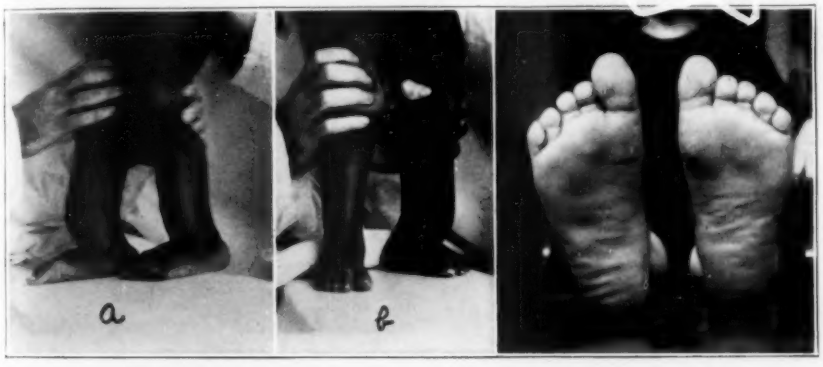


Fig. 6.—A, rachitic flatfoot, with anterior bowed tibia; B, another view of the same subject. C, the feet, not yet deformed by shoes, of a girl, Czecho-Slovakian, aged 18.

between the scaphoid and cuneiform and between the scaphoid and astragalus, the scaphoid and os calcis and the astragalus and os calcis. The ligament between the cuboid and the os calcis is contracted. There is gaping of the bones on the inner border of the foot, namely, scaphoid, os calcis, astragalus and first cuneiform. There is compression of the

bones on the outer border of the foot, namely, cuboid, os calcis and astragalus. The bones of the midtarsal region are found rotated downward and inward, especially the scaphoid and first and second cuneiforms. The forepart of the foot is abducted, the foot is everted and is therefore in valgus position.

The associated pathology often reveals that the general condition of the child is below par muscularly; there may be a generalized amyotonia. Knock-knee is more common than bow-leg. A round back is frequently present. The mother says the child does not walk properly, is awkward

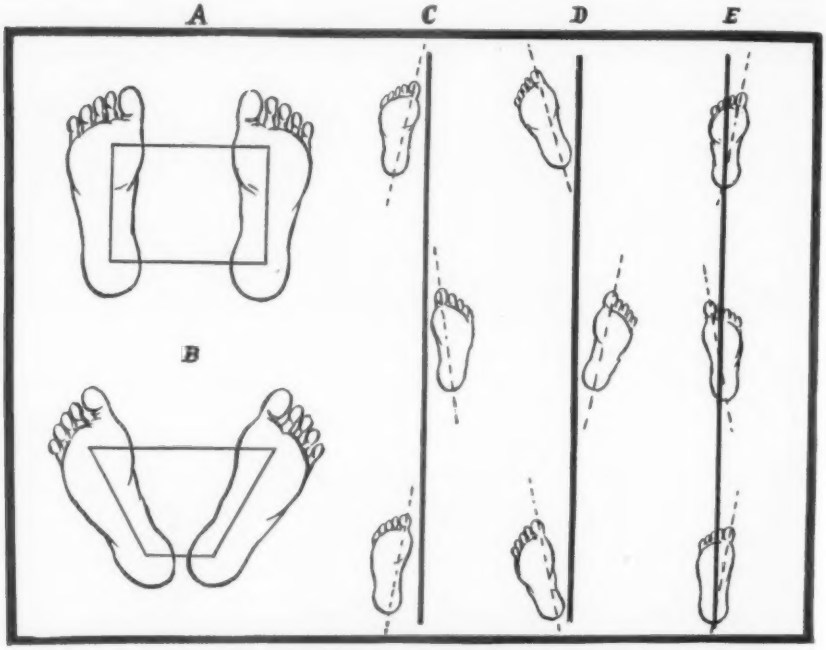


Fig. 7.—A, four square position, standing, which is correct; B, military position, standing, incorrect; C, four square position, walking, correct; D, military position, walking, incorrect; E, Indian position walking (T. S. Ellis).

and that the ankle bones protrude. There seems to be a bone displaced (scaphoid or sustentaculum tali), the child's ankles "interfere" and the child complains of early fatigue, has "weak ankles," and runs the shoes over unnaturally. The child does not want to run and play. Pain is usually absent because the foot is flexible. If arthritis should develop, decreasing the flexibility, a rigid valgus foot results in a disabling deformity.

Objectively, on front view pronation is seen, that is, downward and inward rotation of the midtarsal region, abduction of the forefoot and

eversion; in other words, a valgus deformity. A plumb line dropped from the middle of the patella falls inside the normal point. On rear view, the medialward curving of the Achilles tendon the so-called Helbing sign is seen. A plumb line dropped from the middle of the popliteal space is not parallel with the Achilles tendon. The heel is flattened and rotated, in some cases producing the "heel of an ape." The prominence of the scaphoid region can be seen from behind. It is possi-

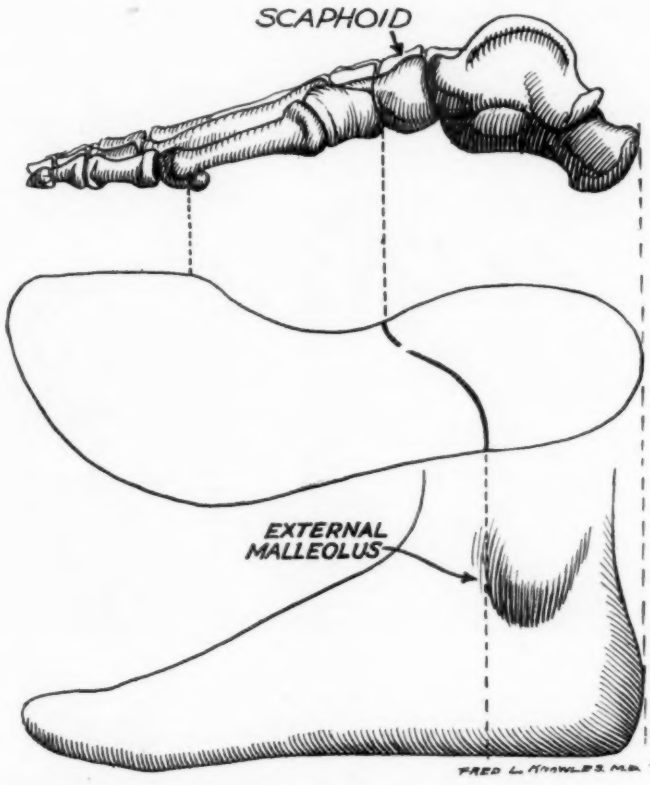


Fig. 8.—Inner and outer border measurements of H. O. Thomas heel.

ble to have one valgus and one varus deformity, namely, a flatfoot on one side and a clubfoot on the other.

The value of footprints has been overestimated both from the standpoint of diagnosis and progress. The print of the new-born infant is misleading in that it usually looks flat. In fact, the foot of a new-born infant, if cross sectioned, will reveal a definite bony arch obliterated by a fat pad. One may find a foot with a high arch but in a position of pronation to which the term pes cavus valgus may be applied.

DIAGNOSIS

The diagnosis of flatfoot should not be difficult. The various conditions which very infrequently must be differentiated are: injury, toxic arthritis, synovitis, bursitis, tendinitis, infantile paralysis, Kohler's tarsal scaphoiditis, apophysitis of os calcis and tuberculosis. The prognosis in flat foot is very good, depending on how well the parent or governess carries out the treatment. In the rigid type the course is protracted and the prognosis is guarded. Whitman says that it usually requires one year for a cure, but the shoes need attention indefinitely.

TREATMENT

The indications for treatment are to teach proper walking, to increase the power of the supporting structures, to increase the local circulation,

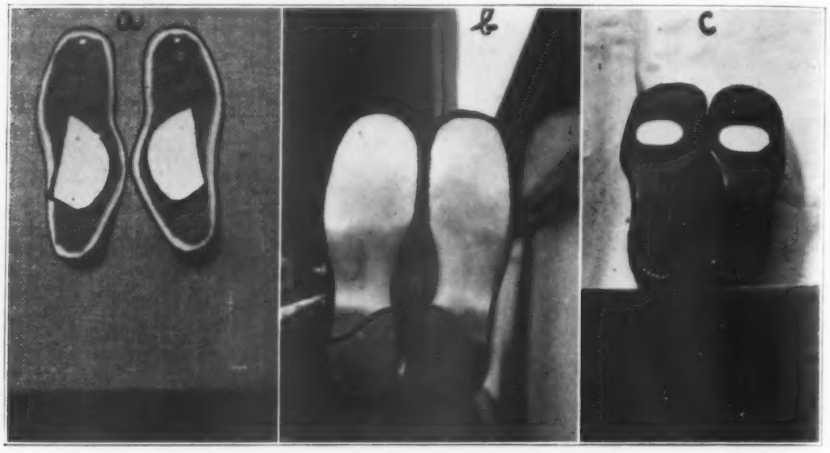


Fig. 9.—A, felt pads for longitudinal arches, glued to leather insoles; B, modified heels of H. O. Thomas; C, same as B.

to support the weakened structures, to produce supination and to correct the associated pathology, such as knock-knee or bow-legs, etc. The methods of meeting these indications are prescribing proper shoes, exercises, massage, contrast foot baths, felt pads, plaster-of-Paris casts and operation.

The child should be taught to walk with the feet parallel or toeing in slightly. It should come down on its heels, tilt its weight to the outer borders of the feet and come up on the toes with a spring. The shoe should only rarely be "made to order." It should be a well fitted, laced shoe; not a half shoe. The most important measurement is from the back of the heel to the middle of the big toe joint, which should be opposite the point at which the shank joins the ball of the sole. Next, the shoe must grasp the heel; it must not be too wide at the heel and

through the shank, and should allow for rapidly growing feet. The use of a fluoroscope in fitting shoes is of great value.

Shoes.—Flexible shank shoes are indicated when the patient needs only exercise; but most of the patients brought to the orthopedic surgeon need both exercise and support, and the latter need is not supplied except by a rigid or semirigid shank. It is analogous to a bridge sagging in the middle. The insertion of a Steinbrecker corrugated metal shank makes a flexible shank shoe very satisfactory for the preliminary shoe. It should be discontinued when the feet improve in strength.

The modification of the shoe consists chiefly in the application of a Thomas heel, devised many years ago by an orthopedic surgeon of Liverpool, which to date has been modified but never improved. Each child must be measured for this heel. There are four dimensions; the inner border length, from the tip of the os calcis to the anterior border of the scaphoid tubercle; the outer border length, from the tip of the os calcis to a perpendicular line dropped from the anterior border of the external malleolus; the inner border height, from one eighth to one fourth of an inch higher than the normal height of heel, and the outer border height, the normal height of heel for the subject's shoe. The imitations so frequently seen of this heel are very poor. The function of this heel is to compel the child to walk over the outer border of the foot, and, when properly made, it forces him to a proper walking angle. Only infrequently should the sole be tilted. Reinforced uppers for "weak ankles" are used occasionally as a temporary measure. It is important that the leather reinforcement be carefully molded over the malleoli, or pressure areas will result.

Gymnasium shoes should be worn for that purpose only. They should include the ankle, and have felt pads inserted. Ballet slippers should not be worn except while dancing. They too can be padded.

The child must not go barefoot except in the sand or on soft ground. During convalescence from any illness, it is very important that the child's feet be supported at all times during weight bearing, because it is a period of relaxation of supporting structures of the arch.[1] Never allow bedroom slippers.

Exercises.—Exercises are the most important factor in the treatment. They are active and resistive, and should be carried out twice daily in bare or in stockinged feet. The child is told they are games. Exercises must be done slowly, and the feet should never be allowed to "come down with a bang." A great many special exercises have been described. Some of the most valuable are given.

---

1. Lewin, Philip: Do Your Feet Hurt? Hygeia **3**:317 (June) 1925.

EXERCISES

1. Stand barefooted with the feet parallel, and about 2 inches apart, straddling a seam or a line in a rug. On the count of 1, the feet are forcibly turned out, so that weight is borne on the outer borders, and on the count of 2, they are allowed to slowly roll in, but not all the way. This is carried out from 25 to 100 times.

2. Same as number 1, except that the two big toes are held together and on the floor.

3. Standing with the feet straddling a seam in the rug, or a line on the floor, the subject walks across the room with all the weight borne on the outer borders of the feet. This is carried out five times up and back.

4. The same as exercise 3, except that the subject lifts the foot so that it is opposite the other knee, and walks across the room in that way, that is the so-called "ostrich step." Weight must at all times be borne on the outer border of the foot.

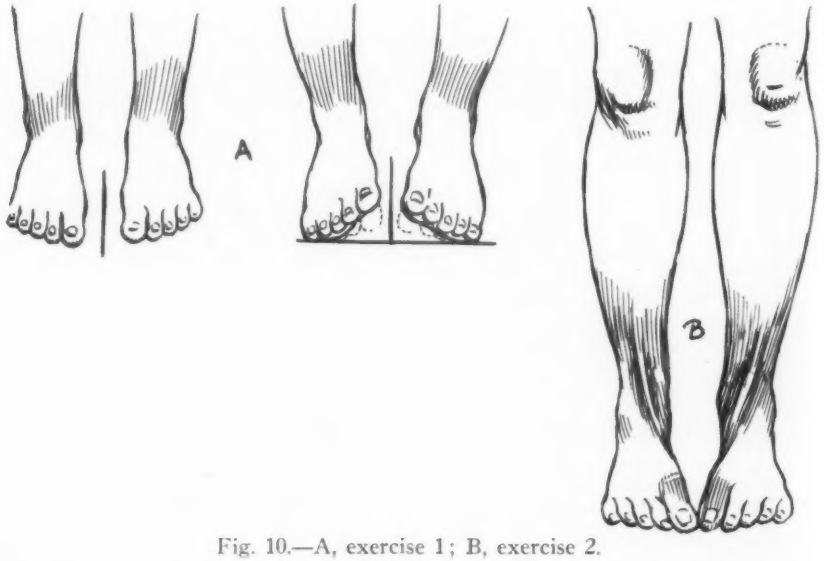


Fig. 10.—A, exercise 1; B, exercise 2.

5. The feet are held parallel, and the knees are maintained in a straight position. The knees are then rolled outward, which automatically causes the longitudinal arch to rise (Lowman). This is carried out about 25 times.

6. Rise on the toes, tilt the weight to the outer borders and come down—in 2 counts. This should be done 25 times.

7. A supination board is an isosceles triangle board, about 6 inches high and 8 feet long. The child walks the length of the board three or four times, as one would walk on the eaves of a house.

8. The subject is seated, holding the foot at a right angle with the leg, and not turned in or out. The exercise is done in four counts. On the count of 1, the foot is forcibly put in the position of toe-drop. On the count of 2, the foot is swung in; on the count of 3, it is pulled upward, and on the count of 4 it is brought back to the starting position describing a half circle. This is performed 25 times.

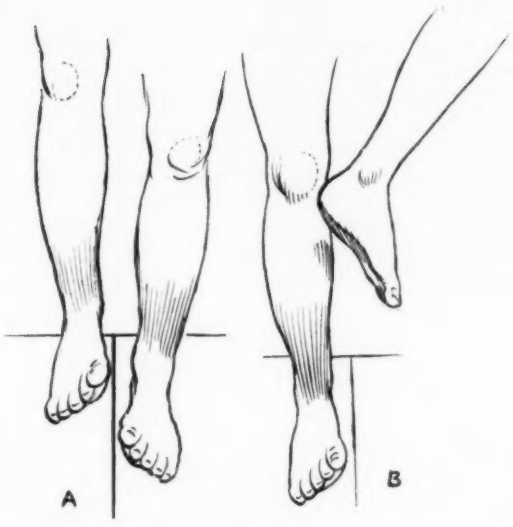


Fig. 11.—A, exercise 3; B, exercise 4.

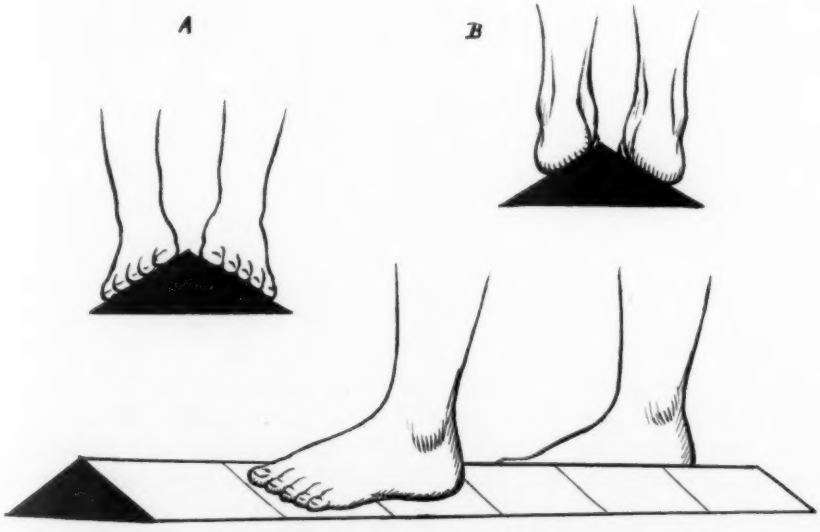


Fig. 12.—Supination board, which consists of an isosceles triangle 6 inches high, and 8 feet long. A, front view; B, rear view; C, side view.

9. This is a resistive exercise. The subject sits on a table and the second person sits on a chair. The subject forcibly swings his foot inward and upward, and holds it in this position with all his power. The second person attempts to swing the foot outward and downward. This effort on the part of the second person is resisted by the subject. The exercise is carried out from 15 to 25 times. At no time should the second person use as much power as the first. Between each two of these exercises the subject relaxes his foot.

10. (For shortened heel tendons).—Standing about 2 feet from a wall, with the toes together and heels apart, the palms are placed against the wall, and the back and hips are allowed to sag in; at all times the heels must be kept on the ground. This should be done about 25 times, and the distance from the wall gradually increased as the heel tendons stretch and will permit.

11. Walk on the heels across the room twice.

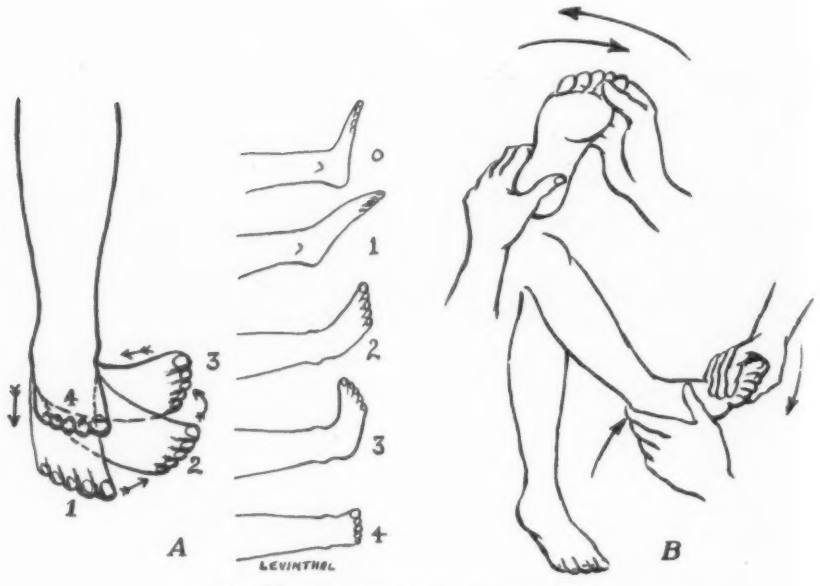


Fig. 13.—A, exercise 8; B, exercise 9.

OTHER EXERCISES

Ballet dancing is excellent exercise because of the foot training, although much of it is very hard on the longitudinal arch at first. There are, however, some children for whom it is detrimental until their feet have been strengthened by the treatment outlined here. Ballet dancing may be started at the age of 4 or 5 years, toe dancing should not be started before the age of 8 or 10 years.

Swimming is very good. Roller skating is good, but ice skating may be harmful at first. The child should wear a wide figure-of-eight webbing or leather strap over the stocking, or a leather skate strap outside of shoe, making a figure 8.

Kiddy cars may be injurious in causing knock-knee and flatfoot. It is important that the distance from the seat to the ground is correct for the individual child. If the child wears out the shoe on the inner border, it is harmful.

Massage of the feet and legs should be given twice daily, using olive oil or cocoa butter. The movement should be deep rotary. In the case of painful feet in the older children an anodyne ointment should be used:

	Gm. or Cc.
℞ Olei gaultheriae	4
Acidi salicylici	4
Mentholis	4
Phenolis	1
Ungt. aquae rosae	25
Lanolin	25

Mix and make an ointment, and put in collapsible tube.
Sig: Apply externally for massage twice daily using deep rotary movement.

Fig. 14.—A, flatfoot in a girl, aged 1 year; B, same as A, showing a positive Helbing sign; C, same feet in corrective plaster-of-Paris casts.

Contrast foot bathing should be prescribed for older children; the directions are as follows:

Obtain two buckets, each large enough to contain both feet. Fill bucket no. 1 about two-thirds full of warm water, and bucket no. 2 two-thirds full of cool water. Sit beside the buckets. Place both feet in the warm water for exactly one minute. Remove feet and place in the cool water for exactly one minute. Alternate in this manner for ten minutes, that is, five minutes in each bucket. This routine should be carried out twice a day, increasing the contrast of the water gradually from day to day.

Support for the longitudinal arch is obtained by means of felt pads. These afford a resilient support and thereby increase the spring of the gait. They are highly desirable and perferable to rigid supports such as those made of metal, celluloid or leather. Metal arch supports act as props or crutches and do not increase the power of the supporting structures of the foot.

I have long since discontinued the use of leather insoles because they confuse the shoe fitter, who cannot judge accurately the amount of space to be allowed. He is instructed to fit the foot accurately without

allowing for anything. The pads should go into natural hollows, therefore, no extra space is required. The pads are inserted directly into the shoes and held by means of a special glue and tacks.

A Goldthwaite figure-of-eight leather strap is of some value. Adhesive strapping is only occasionally indicated, except in acute traumatic feet. Plaster-of-Paris is necessary in some cases, and is usually better than braces for short periods. Dr. Silver of Pittsburgh recommends plaster over comparatively long periods, in an attempt to cause a certain degree of rigidity in a varus position. The braces which should be mentioned are the single outside caliper and T strap of Jones, and the lever-sole of Calot.

Fig. 15.—a, b and c, Calot lever sole applied to shoe; d, e, f, g, h, and i, the same applied to the foot.

Operation is rarely indicated except for rigid flat feet, in which type forcible manipulation under anesthesia and the application of a corrective plaster cast is of great value. Occasionally, the peroneal tendons must be resected. Lengthening of the Achilles tendon is indicated in the so-called "muscle bound" feet, because these patients are unable to perform the exercises properly owing to the structural shortening of the tendon. Osteotomy of the os calcis or other bones is occasionally indicated. Tendon transplantation is advisable in selected cases as is also partial arthrodesis. The treatment of associated knock-knee or bowleg (if marked) is osteotomy and corrective casts, or braces.

I have not referred to metatarsalgia in childhood, or metatarsus varus, because they do not come within the scope of this paper.

Correspondence

ACIDIFIED MILKS

To the Editor:—In my review of acidified milks, in the March issue of the *American Journal of Diseases of Children*, I failed, through an oversight, to give credit to Dr. Roy M. Greenthal of Milwaukee, who appears to have been the first in this country to use milk soured by additions of acid for infant feeding. In a paper read in June, 1922, and published in January, 1923 (Greenthal, R. M., The Role of Acidified Milk in Infant Feeding, *J. Michigan M. Soc.* **22**:9 [Jan.] 1923), Dr. Greenthal reported the successful use of milk soured by the addition of from 6 to 8 cc. of pure lactic acid to the quart of milk, approximately the proportions later advised by Marriott. Dr. Cowie referred to Dr. Greenthal's work in his discussion of my paper at the 1923 meeting of the American Pediatric Society.

HAROLD K. FABER, M.D., San Francisco.

Stanford University School of Medicine.

News and Comment

DEATHS OF PEDIATRICIANS ABROAD

We have to record the following deaths among pediatricians abroad.

Prof. André Moussous of Bordeaux at the age of 69. Dr. Moussous had been for many years a prominent teacher of pediatrics at Bordeaux, and had published many articles on various pediatric subjects.

Prof. A. Filia, Director of the Pediatric Clinc of the University of Sassari, Italy.

Dr. Chatin of the Faculty of Medicine of the University of Lyons, France. Dr. Chatin took an active interest in puericulture and was especially helpful in forwarding the efforts of the American Red Cross of Lyons. He took over the visiting nurses work, established by that organization, and has conducted it very successfully ever since.

BREAST FEEDING DEMONSTRATION

The Massachusetts Department of Health requests the cooperation of the medical profession in the establishment of breast feeding demonstrations in four cities and towns, which have been selected because the public health nursing is well organized in those communities. The object is to show that it is possible and desirable to increase the percentage of breast fed babies, the plan is to secure the consent of each physician to have their patients visited by a public health nurse who will see every mother two weeks after the birth. A "form" as a reminder of breast feeding will then be sent to the mother monthly, and will include a return form; every mother who fails to return the form or signifies thereon any difficulties in feeding will be visited by the nurse, and every mother will also be visited when the baby is six months of age.

Abstracts from Current Literature

Anatomy and Physiology

FURTHER STUDIES ON THE PARATHYROID HORMONE. SECOND PAPER. J. B. COLLIP and E. P. CLARK, J. Biol. Chem. **66**:133, 1925.

The authors have isolated the hormone of the parathyroid gland of oxen as a light gray amorphous powder; it was soluble in water, and precipitated at a hydrogen ion concentration of p_H-4.8. It is apparently a protein containing 14.6 per cent to 15.5 per cent nitrogen, some sulphur and iron and no phosphorus; it gives the common protein reactions. The purified substance contained 1 unit per 0.3 mg. The method of production of the purified preparation is given.

THE CONCENTRATION OF CHLORIDES IN THE GLOMERULAR URINE OF FROGS. J. T. WEARN and A. N. RICHARDS, J. Biol. Chem. **66**:247, 1925.

The authors examined and compared the chloride content of bladder urine, glomerular urine and blood plasma, obtained essentially simultaneously from individual frogs. The authors used their recently described technic for catheterizing a glomerulus, obtaining approximately 1 mg. urine per hour over a period of four or five hours. Prof. T. W. Richards of Harvard had developed a method for detecting chloride in concentration of 1 : 30,000,000; this method was used in this study. The authors found that the chloride of the glomerular urine was invariably of higher concentration than that of bladder urine, which indicates that the chloride is eliminated by the glomeruli and reabsorbed by the tubules. The concentration of the chloride of glomerular urine was greater than that of blood plasma, simultaneously obtained. The authors believe that errors of technic are not responsible for this difference, and are forced to conclude that filtration is not the only method of glomerular excretion of chlorides.

STUDIES ON CHOLESTEROL. I. SYNTHESIS OF CHOLESTEROL IN THE ANIMAL BODY. F. S. RANDLES and ARTHUR KNUDSON, J. Biol Chem. **66**:459, 1925.

White rats were fed on a diet containing no cholesterol for a period lasting from time of weaning until 5 months of age. Analysis of the blood, brain and liver and in some cases of the entire body of these animals showed cholesterol to be as abundant as in control animals. Thus, the white rat is able to synthetize cholesterol.

THE DETERMINATION OF CALCIUM IN TISSUES, FECES, AND MILK. R. C. CORLEY and W. DENIS, J. Biol. Chem. **66**:601, 1925.

In the analysis of bone, of other body tissues, of milk and of feces, the authors have substituted for the usual method reducing to ash a new procedure in which the material is digested in an autoclave at temperature of 160 to 180 F., with from 0.01 to 0.1 normal solution of sodium hydroxide. The material after digestion is then treated for thirty minutes with excess of concentrated hydrochloric acid and filtered. The calcium is in the filtrate, and is determined volumetrically after precipitation as oxalate.

THE FATE OF SUGAR IN THE ANIMAL BODY. I. THE RATE OF ABSORPTION OF HEXOSES AND PENTOSES FROM THE INTESTINAL TRACT. CARL F. CORI, J. Biol. Chem. **66**:691, 1925.

Solutions of various hexoses and pentoses were fed to fasting rats by stomach tube at hourly periods. The rats were then killed and the intestine ligated and removed. The amount of unabsorbed sugar in the intestine was determined per unit of body weight.

Each sugar is absorbed at a definite rate, which is independent of concentration or total amount. Thus 20, 50 and 80 per cent glucose solutions are absorbed at the same rate.

The following is the order of the sugars in the rate of absorption: galactose, glucose, fructose, mannose, xylose, arabinose.

Hypertonic sugar solutions are diluted in the stomach by excretion of water.

HIGGINS, Cincinnati.

MECHANISM OF PANCREATIC DIGESTION. THE FUNCTION OF SECRETIN. J. MELLANBY, J. Physiol. **60**:85-91, 1925.

Pancreatic juice secreted after intravenous injection of secretin contains approximately 0.14 sodium bicarbonate, but diminished quantities of trypsinogen, amylase, and lipase as secretion proceeds. This is not due to exhaustion of the gland. Removal of vagal control from the pancreas cells by atropine or by section of the vagi produces the same effect. Hence, the hypothesis that the enzymic content of pancreatic juice is determined by the vagus nerves, whereas the quantity of sodium bicarbonate is determined by secretin.

CELLULAR CHANGES IN INTESTINAL FAT ABSORPTION. W. CRAMER and R. J. LUDFORD, J. Physiol. **60**:342--346, 1925.

In the synthesis of fat which proceeds in the cells of the intestinal epithelium during fat absorption, the Golgi apparatus is the cell structure mainly concerned.

NORMAL VARIATIONS OF INORGANIC PHOSPHORUS OF BLOOD. R. E. HARVARD and G. A. REAY, Biochem. J. **19**:882, 1925.

During sleep, night or day, the rise in inorganic phosphorus may be from 20 to 50 per cent. Seasonal variations range from 2.9 mg. per hundred cubic centimeters in January to 4.0 mg. per hundred cubic centimeters in August (adults).

OBSERVATIONS ON THE EFFECT OF VARIOUS CARBOHYDRATES ON THE KETOSIS OF STARVATION IN THE HUMAN SUBJECT. M. W. GOLDBLATT, Biochem. J. **19**:948-957, 1925.

Glucose, fructose, sucrose and maltose have an antiketogenic action, while galactose, mannose, lactose and glycerol are inert. Evidence is shown for deficiency in storage power and oxidation after starvation. The normal condition is reestablished after administration of cabohydrate. The maximum antiketogenic action of the sugars has been shown to occur during the fall in blood sugar, that is, during storage and oxidation of sugar.

KUGELMASS, New York.

THE ABSORPTION BY THE MUCOUS MEMBRANE OF THE URETHRA AND BLADDER. W. SCHÖNFELD and W. G. MÜLLER, München. med. Wchnschr. **72**:291-294, 1925.

The authors describe a case of alypin intoxication and death followed by an injection of 10 cc. of a 5.0 per cent solution of alypin nitricum into the urethra; one-half minute later the first symptoms were noted, nausea and tonic-clonic convulsions; one-half hour later, death. According to the necropsy findings, death was due to an acute intoxication.

Following this, the authors undertook experiments to obtain information about the absorption of drugs through the anterior and posterior parts of the urethra and the bladder. They used 10 cc. of a 5.0 per cent pilocarpin solution which was kept in the urethra for fifteen minutes. For the posterior urethra they used from 10 to 20 cc. of the same solution and they injected 300 cc. of a 0.5 per cent solution into the bladder.

Tuberculin in 1 per cent, 10 per cent and 20 per cent solutions was used for the same purpose in cases of tuberculosis of the skin. In three cases out of five, they observed focal and systemic reactions similar to those they had previously from subcutaneous tuberculin.

For the pilocarpin absorption the salivation was used as an index.

The anterior and posterior parts of the urethra absorbed a considerable amount of both drugs. (No quantitative studies were made.) The bladder experiments were negative, but they did not accept this as a proof, because only a 0.5 per cent solution had been used.

Further experiments were undertaken to determine whether irritation has any influence on the absorption, and they found that absorption was greater after irritation, even after hours of time had elapsed.

GROB, Rochester, Minn.

HYPNOSIS IN OTOLARYNGOLOGY. Proceedings of the German Otolaryngological Society, Part 2, Supplement. ALFRED PEYSER, Ztschr. f. Hals-, Nasen- u. Ohrenh. **12**:214, 1925.

Peyser believes there is a definite place for hypnosis. He suggests reeducating and activating the weakened will, but, if all these psychotherapeutic ends fail, hypnosis, superficial or as deep as necessary, may succeed. He classifies suitable conditions as follows:

1. Local functional disturbances, combined with or following organic disturbance, that is, unusually severe pain; neuralgia after healing; posttonsillectomy trismus; postoperative aphonia.

2. General disturbances: insomnia from tinnitus; loss of appetite from cacosmia.

3. Mental states or complexes induced by illness such as ozena, deafness and speech defects.

4. Phobias: syphilis, carcinoma and hereditary deafness.

5. Habits: ear scratching; nose picking; drug addictions.

6. Fear: of anesthesia; of operation. Removal of fear may enable use of local instead of general anesthesia.

Hofer has found it useful in nervous cough. Stern believes suggestion and reeducation are preferable to hypnosis in stuttering. Kuemmel sees danger in systematic hypnosis for tinnitus. Peyser also had good results in nervous cough. He agrees with Stern that hypnosis is not the best method for stuttering. He does not recommend it for tinnitus but for anxiety neurosis and insomnia resulting therefrom.

LEWY, Chicago.

Pathology, Bacteriology and Biochemistry

THE EFFECT OF THYROPARATHYROIDECTOMY IN DOGS ON THE EXCRETION OF CALCIUM, PHOSPHORUS, AND MAGNESIUM. ISIDOR GREENWALD and JOSEPH GROSS, J. Biol. Chem. **66**:185, 1925.

The authors found no increase in the calcium excretion in urine and feces of dogs after thyroparathyroidectomy. This is contrary to findings in earlier work reported by McCallum.

A COLORIMETRIC METHOD FOR THE DETERMINATION OF THE p_H OF CEREBROSPINAL FLUID. IRVINE MCQUARRIE and A. T. SHOHL, J. Biol. Chem. **66**:367, 1925.

The authors have developed a colorimetric method for determining the hydrogen ion concentration (p_H) of cerebrospinal fluid. In such determinations special care must be taken: (1) to avoid loss of carbon dioxide from the fluid, and (2) to make the determination at body temperature.

The blood and spinal fluid normally have the same p_H. The spinal fluid of patients with meningitis is more acid than the blood.

A METHOD FOR THE DETERMINATION OF THE ENERGY VALUES OF FOODS AND EXCRETA. FRANCIS G. BENEDICT and EDWARD L. FOX, J. Biol. Chem. **66**:783, 1925.

This is a simple method for obtaining the caloric value of food and excreta by determining the oxygen consumption in the combustion of the material and calculating the caloric value by using the average factor that 4.85 calories equals 1 liter of oxygen consumed. (Fat = 4.7 calories, starch = 5.06 calories.)

The material is burned in a small glass chamber attached to the Benedict-Collins respiration apparatus; the apparatus is filled with oxygen; ignition is by iron wire as in a bomb; the change of volume of the entire system represents the oxygen used in the combustion (CO_2 being absorbed by soda lime).

HIGGINS, Cincinnati.

THE RELATION OF BACILLUS ABORTUS FROM BOVINE SOURCES TO MALTA FEVER. THEOBALD SMITH, J. Exper. Med. **43**:207, 1926.

The essential identity of *B. abortus* and *B. melitensis* pointed out by Evans has been affirmed by all those who have subsequently compared them. The problem to be solved concerns the minor differences which make one pathogenic for man, the other not, except under unusual conditions still to be defined.

Two strains of *B. melitensis* isolated from human cases, and strains of *B. abortus* of bovine and porcine origin were inoculated into guinea-pigs. The lesions produced in the guinea-pigs were studied.

The author's conclusions are:

1. Comparative tests on guinea-pigs with *B. abortus* yield the best results when minute doses are injected subcutaneously and the animal kept for at least four weeks.

2. *B. abortus* gradually loses its virulence for guinea-pigs under artificial cultivation.

3. Two cultures resembling *B. abortus* from cattle, isolated from human cases of so-called Malta fever, are shown to be in their effect on guinea-pigs not identical with the bovine strains.

4. The results of studies of *B. abortus* from swine indicate a close relation between the porcine strains and the two human strains.

AGGLUTINATION AFFINITIES OF THE ABORTUS-MELITENSIS GROUP OF BACTERIA, WITH SPECIAL REFERENCE TO TWO HUMAN STRAINS. MARION L. ORCUTT, J. Exper. Med. **43**:225, 1926.

In view of the differences between *B. abortus* of bovine origin and two human strains resembling *B. melitensis* described by T. Smith, it seemed desirable to examine the serologic relations of the strains compared by him with especial reference to agglutination.

Two strains each of *B. abortus* of bovine origin, *B. melitensis* from human cases, and *B. abortus* from swine were tested. No serologic distinctions were demonstrated. The *B. melitensis* strains were found to be identical with the bovine and swine strains by means of agglutination and agglutinin absorption reactions in unheated serums, by agglutination in heated serums, and with the use of heated cultures in unheated and heated serums.

McCLURE, Evanston, Ill.

METHODS FOR INCREASING THE PRODUCTION OF ANTITOXINS. G. RAMON, Ann. de l'Inst. Pasteur **40**:1 (Jan.) 1926.

In an attempt to enhance the antitoxic value of serum, it was noted that when abscesses resulted from inoculation of the antigen, due to skin contaminants, the titer was increased. In order to avoid the complications introduced by the contaminants, and still retain the stimulating effect, sterile foreign substances were mixed with the anatoxin before inoculation. Tapioca was found suitable, and by gradual liberation of the anatoxin, it seemed to prolong its effect. In a large series treated in this manner, the titer of the antibodies at the close of the period was from two to five times as great as in a control series which received the same amount of anatoxin, but without the addition of foreign substances.

HYPERSENSITIZATION TO TUBERCULIN AND TO KOCH'S BACILLUS IN EXPERIMENTAL TUBERCULOSIS. A. BOUQUET and L. NEGRE, Ann. de l'Inst. Pasteur **40**:11 (Jan.) 1926.

Summarizing a lengthy review of experimental work, these authors arrive at the following conclusions:

Tuberculous hypersensitization, which is responsible for the reactions to the various tuberculin tests, can be produced by the paratuberculous bacilli and their extracts, in addition to the various types of Koch's bacillus and their tuberculins.

In most species of animals, particularly in the guinea-pig, the reactions which indicate this hypersensitization present numerous aspects: the infected animal soon responds to the intraperitoneal, intravenous or subdural reinoculations with an immediate anaphylactic shock; later with generalized progressive disturbances, capable of producing death within a few hours. Locally, after the intradermal test, one sees first a transitory papule, followed by necrosis and suppuration, sometimes resulting in a superficial slough. Normal non-sensitized persons react to neither the bacillary proteins nor to the tuberculin.

The living tubercle bacilli, whether virulent or not, or tuberculin-producing or not, as well as the dead bacilli, whole or disrupted, or with proteins, all sensitize rabbits and guinea-pigs in varying degrees to the dead bacilli, their homologous proteins, and to tuberculin. The liberated proteins represent the essential antigen of Koch's bacillus, while tuberculin is a partial antigen, passive, and unique in its action.

After a greater or lesser delay (the ante-allergic period), tuberculous guinea-pigs react to tuberculin and to dead bacilli. However, since this response can be evoked in varying degree by avirulent bacilli, the dead organisms or their proteins, it would appear that a nodular tuberculous lesion is not necessarily the cause of this sensitivity.

In the tuberculous person, hypersensitivity and immunity usually coexist. In all instances, the former precedes the latter in its development; and in animals prepared by the injection of dead bacilli, or avian or paratubercle bacilli, the hypersensitivity is not accompanied by any significant degree of immunity to Koch's bacillus.

Immunity and hypersensitivity are, therefore, two distinct and independent conditions, arising in an organism infected with Koch's bacillus.

INFLUENCE OF SPECIFIC IMMUNE SERUMS ON THE CULTURE OF PATHOGENIC ORGANISMS. M. NICOLLE and E. CAESARI, Ann. de l'Inst. Pasteur **40**:43 (Jan.) 1926.

It has been noted that organisms may grow better in mediums which contain serums of animals immunized to the organism in question than in culture mediums containing nonimmune serum. This has been confirmed by the authors, and found to apply to many organisms, including the gonococcus and pneumococcus (groups I, II and III) and *B. anthracis, B. diphtheriae, B. tetani, B. typhosus* and *B. paratyphosus A.* In all cases in which liquid mediums were used, the culture obtained was more abundant when the medium contained the specific homologous antiserum than when it contained nonspecific antiserum or normal horse serum. There is increased tendency for the organisms to clump together, because of agglutination, and it is suggested that this property may serve to concentrate at the surface of the organism the nutrient constituents of the medium needed for bacterial growth. When solid mediums are used, no increased growth is noted.

BOYD, Iowa City.

CONTRIBUTION TO THE STUDY OF TERATOMA OF THE THYROID. HUGO CUSTER, Frankfurt. Ztschr. f. Path. **33**:125, 1925.

The author reviews eight cases in the literature, all but one of them occurring in new-born children, the exception being a woman aged 41. His own case was in a child, aged 3 days. The tumor was made up of: 1. Glia tissue, which composed the bulk of the growth. 2. Cysts with cornified epithelium, hair follicles, sebaceous glands, etc. 3. Connective tissue, partly fibrillar and partly myxomatous in nature. 4. Hyaline cartilage. 5. A little cancellous bony tissue. 6. A small amount of fat. 7. Cysts with cylindric epithelium. He discusses the various theories as to the origin of such tumors from the earliest (Wilms, Marchand, etc.) to the latest and believes that Budde's theory (that thyroid teratomas represent displaced elements of the foregut) is the most plausible; although he considers as somewhat artificial, that author's further assumption that entire blastomeres are included in the thyreoglossal duct, or in a gill cleft. Custer believes that such tumors are purely a matter of chance displacements of totipotential cells from the foregut, structures that can reproduce any or all of the three germ layers.

FOOT, Cincinnati.

SOME RARE BACTERIOLOGIC FINDINGS IN SECRETIONS AND EXCRETIONS. L. BITTER and M. GUNDEL, München. med. Wchnschr. **72**:379-380, 1925.

In four cases, the authors found that a bacillus which they named *Bacillus septicum* was the causative agent of pus formation and sepsis. Morphologically and culturally, it occupies a position between malleus and diphtheroid bacilli. In two cases, it caused otitis media; in two other cases, it produced purulent meningitis. Two blood cultures were taken with positive results. Three occurred in young children, but the age of the fourth was unknown.

In the exudate of one adult with pleuritis, they found diphtheroid pyogenes flavum bacilli. In the blood of another adult with phlegmon and icterus, *Bacillus fecalis-alkaligenes* was found, together with a streptococcus. The *bacillus fecalis-alkaligenes* proved pathogenic in the animal experiment.

EXPERIMENTAL STUDIES CONCERNING THE ACTION OF STRONTIUM AND ITS CORRELATION TO THE DYNAMIK OF THE HEART AND IONIC MILIEU. F. SALZMANN and F. HAFFNER, München med. Wchnschr. **72**:550-551, 1925.

In a comparative study, strontium was found to have a similar but stronger action on the heart than calcium. When calcium is replaced by strontium in a Ringer nutrient solution, the heart contractions become more marked; on returning to a normal Ringer solution the opposite happens. Higher concentrations of calcium tend to produce disturbances of the heart rhythm even up to blocking of the heart action; strontium acts in the same way only this tendency is less marked. In a concentration below 1:1000, the action on the heart is only about one-fourth that of calcium, this being due to the potassium ions in the Ringer nutrient solution. The paper gives only a summary of their work which will appear in the *Archiv für experimentelle Pathologie und Pharmakologie*. Salzmann will report at a later date about therapeutic experiments and results.

GROB, Rochester, Minn.

INFLUENCE OF IONS UPON DIURESIS IN INFANTS. E. FREUDENBERG, Ztschr. f. Kinderh. **39**:608, 1925.

In strongly acid urine, measured by its hydrogen ion concentration, granular casts occur and disappear when the urine becomes less acid. In the toxic form of acute disturbance of nutrition, the occurrence of casts in the urine represents one of the signs of acidosis.

INFLUENCE OF IONS ON THE MEANING OF IDIOMUSCULAR SWELLINGS IN YOUNG CHILDREN. F. DEMUTH, Ztschr. f. Kinderh. **39**:613, 1925.

The phenomenon, which consists of a localized contraction of muscle or twitch, at the site of a mechanical stimulation, has been known for a long time but never described in infants. Moreover, there may appear on stimulation, instead of a twitch, a distinct swelling which remains visible for a short time. If the twitch phenomenon occurs in the first nine months, it is of bad prognostic import. The swelling phenomenon is even more serious. No explanation is available.

EMERSON, Boston.

NEW OBSERVATIONS ON THE ANATOMY OF THE VOCAL CORDS. Proceedings of the German Otolaryngological Society, Part 2, Supplement. M. HAJEK, Ztschr. f. Hals-, Nasen- u. Ohrenh. **12**:220 (Nov.) 1925.

Beneath the epithelium there is a thin propria which lies loosely on the elastic edge of the cord and is definitely delimited above and below at the

point at which the squamous epithelium meets the ciliated. A definitely localized edema can be produced by injection of fluid in this region (Reinke). According to this author, a similarly definitely localized edema occurs in living subjects. Polyps and polypoidal thickening of the edge of the cord margin are the products of chronic inflammation of the distinctly outlined subepithelial tissue, with secondary changes in the same.

LEWY, Chicago.

TITRATION OF DIPHTHERIA ANTITOXIN AND A TESTING OF THE SERUMS USED IN CZECHOSLOVAKIA. B. FEIERABEND, Cas. lek. cesk. **64**:42 (Jan.) 1925.

Practically all the antitoxin and serums are imported, and the Government has not adopted standards for quality. The method of Ehrlich was used and the commercial brands varied from 80 to 105 per cent of the published potency.

STULIK, Chicago.

Nutrition

RICKETS. L. R. DEBUYS, Iowa State M. J. **16**:68 (Feb.) 1926.

Rickets was known 2000 B. C. Glisson described the disease and gave it the name of rachitis in 1681. It was known as English disease because of frequent manifestation in that country.

Virchow showed the chief fault in rickets was lack of proper ossification and not destruction or disintegration. Diagnosis is to be made by its pathologic findings, its roentgenographic evidence and its serologic tests. There has been more investigative work done in the last decade than in any other period.

Several theories are advanced for the cause of rickets, including infection, diet and hygiene. Each is discussed and the results of experiments for each are recited.

This condition is more prevalent the second half of the first year. Breast fed infants showed increased manifestations toward the end of the first year, except craniotabes which began at the fourth week and reached the peak at sixteen weeks.

Calcium and phosphorus are two elements found to be altered in rickets.

In moderate rickets, the phosphorus or calcium or both may be moderately lowered. In severe rickets, the phosphorus is markedly reduced, even in the breast fed, while the calcium may or may not be lowered.

Some observers report two main kinds of rickets, one characterized by normal or nearly normal calcium and low blood phosphorus; the other by normal or nearly normal blood phosphorus, but with low calcium.

A diet defective in its fat content has long been believed to predispose to rickets. This kind of fat is animal fat. The animal fat contains at least one accessory food or vitamin, the fat soluble A.

Cod liver oil is rich in this vitamin. Calcium content of breast milk is greater in mothers of normal infants as compared with milk of mothers of rachitic infants. Calcium content diminishes as lactation progresses. Calcium content is less in the milk of the colored race than of the white race. Egg possesses marked antirachitic properties. Butter fat has a very feeble influence in protecting animals against development of rachitic lesions. Alfalfa leaves and ether extracts from clover blossoms are antirachitic in rats. It has been shown that in rats with rickets a period of fasting induces a cessation of the activity of the disease.

Although there is no longer room to doubt the efficacy of cod liver oil in curing rickets, the nature of the active principle in the oil is still unknown. The

antirachitic effect of cod liver oil is not due to its content of fat soluble A, but to some other factor. The evidence points to a fourth vitamin.

Rickets has been encountered with every kind of food given, and in some instances to an appalling degree in breast-fed infants. Rickets is notably frequent in parts of the world in which the amount of sunlight is relatively small as compared with other parts in which the amount of sunlight is plentiful. Rapid recovery has been noted in many subjects by putting them in the sun and the fresh air without change in diet and without drugs.

Recovery results more rapidly with quartz light irradiation than with any other method. Duration of treatment is different at different ages. Exercise, especially walking, is advised against until the child is well on the road to recovery.

TURNER, Des Moines, Iowa.

THE EFFECT OF FERMENTATION WITH SPECIFIC MICROORGANISMS ON THE VITAMIN C CONTENT OF ORANGE JUICE AND TOMATO JUICE. S. LEPKOVSKY, E. B. HART, E. G. HASTINGS and W. C. FRAZIER, J. Biol. Chem. **66**:49, 1925.

Orange or tomato juice loses its antiscorbutic property within one week after being extracted. This loss of vitamin C is due to the action of oxygen, for when orange juice was protected from air by means of vaseline, its ability to prevent scurvy remained. Orange juice, fermented with yeast, still had vitamin C fifty-one days after being drawn, but had none after one hundred and twenty-six days; the fermentation probably acted to free the juice of oxygen. Bacteria acted very slowly, if at all, to destroy vitamin C. The authors ascribe the absence of vitamin C in sauerkraut and silage to the presence of oxygen.

SOME OBSERVATIONS ON THE RÔLE OF CYSTINE AND CERTAIN MINERAL ELEMENTS IN NUTRITION. ELLA WOODS, J. Biol. Chem. **66**:57, 1925.

White rats, fed exclusively on whole wheat, whole milk powder and table salt, showed a very excellent record as to longevity and reproduction.

THE EFFECT OF CHANGES IN THE CIRCULATION ON CARBOHYDRATE UTILIZATION. F. A. CAJORI, C. Y. CROUTER and RALPH PEMBERTON, J. Biol. Chem. **66**:89, 1925.

Persons with a low sugar tolerance have usually an exaggerated and prolonged hyperglycemia, which may be due to delayed stimulation of the pancreas to insulin production or to an inadequate output of insulin. The delayed removal of sugar from the blood may also be due to interference with the blood supply to the muscle tissues which play a part in the removal of sugar from the blood.

The authors determined the blood sugar curve following ingestion of glucose with the person in two positions: (1) seated, and (2) lying in bed with both legs and one arm elevated. In 54 per cent of the cases the blood sugar remained high over a longer period when the limbs were elevated than in the control tests; in the other cases, there was no change in the blood sugar curve.

These findings were used as a likely explanation of the low sugar tolerance observed in patients with arthritis. For the lowered carbohydrate tolerance is probably due at least in part to the mechanical factor that the blood supply is not so active as normally in the tissues (muscle) which play a large part in the removal of sugar from the blood.

CARBOHYDRATE UTILIZATION. I. RATE OF DISAPPEARANCE OF D-GLUCOSE FROM THE BLOOD. VINCENT DU VIGNEAUD and WALTER G. KARR, J. Biol. Chem. **66**:281, 1925.

This paper contains an experimental study as to the explanation for the effect of diet, fasting and medication on the customary sugar tolerance test used in clinical diagnosis. Rabbits were used as the experimental animals.

Previous periods of fasting cause a slower disappearance of sugar from the blood after absorption from the intestine following giving of glucose by mouth; that is, the blood sugar remains higher over a longer period and there is more tendency to glycosuria if the animal had been starved. If glucose or protein had been fed eighteen hours before the tolerance test, the glucose disappeared more rapidly from the blood; on the other hand, if fat had been fed eighteen hours previously the glucose disappeared less rapidly. If epinephrine was given eighteen hours previously, there was an increased rate in disappearance of glucose from the blood following a test meal, while morphine and insulin cause a decreased rate of absorption. Sodium bicarbonate given during fasting, caused more rapid disappearance of sugar from the blood. The degree of acidosis is not the predominant factor in the rate of disappearance of sugar from the blood.

FAT-SOLUBLE VITAMIN. XXVI. THE ANTIRACHITIC PROPERTY OF MILK AND ITS INCREASE BY DIRECT IRRADIATION AND BY IRRADIATION OF THE ANIMAL. H. STEENBOCK, E. B. HART, C. A. HOPPERT and ARCHIE BLACK, J. Biol. Chem. **66**:441, 1925.

Rats were fed on a diet which produced rickets. The addition of at least 12 cc. of cow's milk daily was necessary to cause recovery of the rats from rickets. However, if the milk was exposed to ultraviolet rays, only 1 cc. was needed for recovery. Similar experiments with goat's milk showed that 0.5 cc. of irradiated milk was equivalent to 12 cc. of unirradiated milk in healing rickets. When a goat was irradiated 1 hour daily for four days, its milk showed healing properties in quantity of 2 cc.

ANTIRACHITIC SUBSTANCES. II. THE ACTION OF N-BUTYL NITRITE ON ACTIVATED CHOLESTEROL AND THE ANTIRACHITIC VITAMIN. CHARLES E. BILLS, J. Biol. Chem. **66**:451, 1925.

n-butyl nitrite destroys the antirachitic property of cod liver oil and also of irradiated cholesterol (dissolved in either seal oil or cod liver oil) slowly at room temperature and rapidly on heating. This presents evidence pointing to the identical nature of these two antirachitic substances.

THE NUTRITIONAL REQUIREMENT OF THE CHICKEN. VI. DOES THE CHICKEN REQUIRE VITAMIN C? E. B. HART, H. STEENBOCK and S. LEPKOVSKY, J. Biol. Chem. **66**:813, 1925.

Chickens fed on a diet containing no vitamin C do not develop scurvy. The livers of such chickens are found to contain an abundant supply of vitamin C.

THE EFFECT OF ORANGE JUICE ON THE CALCIUM, PHOSPHORUS, MAGNESIUM, AND NITROGEN RETENTION AND URINARY ORGANIC ACIDS OF GROWING CHILDREN. MARGARET S. CHANEY and KATHARINE BLUNT, J. Biol. Chem. **66**:829, 1925.

Two growing girls, aged 10 and 11 years, were each put on a fixed diet for two experimental periods of ten and twenty-three days, separated by two and

one-half months. The first part of each experiment was a control period which was followed by a period when 700 cc. of orange juice was added to the diet. Studies were made of the nitrogen, phosphorus, magnesium and calcium balance during a portion of each control and orange juice period.

The orange juice caused:

1. A greater rate of increase in the weight of the children.
2. A greater retention of calcium, phosphorus, magnesium and nitrogen.
3. A decrease in urinary acidity.
4. An increase in organic acids of the urine.
5. A diminution of urinary ammonia.

HIGGINS, Cincinnati.

TREATMENT OF GENERAL DEBILITY. A. B. MARFAN, Nourrisson **13**:221 (July) 1925.

Marfan emphasizes the importance of breast milk in the treatment of these cases. In infants with debility of the third degree, weighing less than 2,000 Gm., it is almost hopeless to try to rear them without it. Marfan advises nine feedings in the twenty-four hours until the weight reaches 2,500 Gm. Such infants should receive a daily supply of breast milk equal to 20 per cent of their weight. In infants for whom breast milk is not available, modified buttermilk is advised, consisting of 1 liter of buttermilk with the addition of 40 Gm. of cane sugar and 10 Gm. of rice flour or farina. The caloric value of this mixture is about 500. A small amount of lime water (10 cc.) is added to each feeding.

In maintaining body temperature, Marfan prefers jackets used for premature infants and hot water bottles to a regular incubator. If the body temperature cannot be raised in this way, hot baths should be given, the temperature of the water being brought to 38 C. and kept there for twenty minutes. After removal from the bath, the baby should be dried and dressed quickly. Stimulation can be carried out by infusions, transfusions into the fontanel and hypodermic injections of caffeine citrate and camphorated oil. Inhalations of oxygen are sometimes helpful. Antisyphilitic treatment is very important when syphilis is present.

McCLELLAND, Cleveland.

A NEW METHOD FOR THE DETECTION OF THE ADULTERATION OF BREAST MILK. H. MEYER, Arch. f. Kinderh. **75**:211 (Feb.) 1925.

A method is described by means of which adulteration of breast milk with cow's or goat's milk, or dilution with water may be detected. The method is successful when only 5 to 10 per cent of cow's or goat's milk is present, or 20 to 25 per cent of water has been added, and can be completed within six to seven minutes, using 10 cc. of milk. The test is performed by titrating the milk against twentieth normal hydrochloric acid solution, the greater amount of buffer substance in cow's and goat's milk binding more of the acid when these have been added to breast milk, and dilution of the milk with water lowering its combining power. As there is a possibility that these two factors might balance each other, an additional check is afforded by the observation of the character and extent of the curd precipitation which occurs with varying amounts of the acid. The character of the curdy precipitate in breast milk is constant for the same person, but varies considerably in different women, and this may prove to be an important factor in its utilization as an infant food.

HEMPELMANN, St. Louis.

HISTOLOGY OF THE LARYNGEAL NERVES. Proceedings of the German Otolaryngological Society, Part 2, Supplement. V. STUPKA, Ztschr. f. Hals-, Nasen- u. Ohrenh. **12**:228 (Nov.) 1925.

Stupka distinguishes large, medium and small medullated fiber bundles; of the last, four varieties. He also describes small nonmedullated nerves, naked axis cylinders and ganglion cells. The article is well illustrated with photomicrographs, and should be read in the original.

LEWY, Chicago.

A CASE OF INTOLERANCE TO COW'S MILK IN AN INFANT WITH PURPURA. M. LANDSBERGER, Ztschr. f. Kinderh. **39**:569, 1925.

No similar case of intolerance to cow's milk with purpura has been described. The thrombopenia, prolonged bleeding time and coagulation time and lack of retraction of the blood clot, were not characteristic of purpura. It occurred in a purely breast fed baby, aged 2 months. Susceptibility to several forms of protein was confirmed by intracutaneous tests which were accompanied by spontaneous hemorrhages.

INFLUENCE OF IONS UPON ANTIRACHITIC ACTIVITY OF THE UNSAPONIFIABLE FRACTION OF COD LIVER OIL. H. BEHRENDT, Ztschr. f. Kinderh. **39**:619, 1925.

Eleven cases of proved rickets were treated with the unsaponifiable fraction of cod liver oil, and its greater curative value was shown in comparison with whole cod liver oil.

MEDICOSOCIAL OBSERVATIONS UPON CHILDREN FED FROM PUBLIC KITCHENS. S. WEISSENBERG, Ztschr. f. Kinderh. **39**:634, 1925.

These observations were made on children during the famine in Russia, in 1922, for the period of a year. The percentage of rickets reported in children, aged from 6 to 10 years, was 20 per cent. Hunger which lasts for months does not do irreparable harm to the body of a child, and compensation occurs quickly when plenty of food is again available. Despite the terrors to which the children were subjected, their health was little affected.

EMERSON, Boston.

Prenatal Conditions

A CASE OF ARACHNODACTYLIA (SPIDER FINGER). NORMAN S. CARMICHAEL, Tr. Edinburgh M. J. **33**:26 (Feb.) 1926.

A girl, aged 2 years, was exhibited at a clinical meeting. She showed numerous congenital abnormalities, chief of which were long and narrow feet and hands, which can be crumpled up dorsally so that the hands touch the back of the forearm. In this condition the muscles are generally poorly developed. The head is dolichocephalic, the face flattened, and the supraorbital ridges prominent and meeting over the nose. There is an anteroposterior ridge on the vertex of the head, and a number of ridges which converge in the external ear. The vision is impaired due to dislocation of the lens, due to a maldevelopment of the suspensory ligament. Usually the eyes do not respond to mydriatics. The chest is rachitic. The mental condition is good.

ASPECTS OF INTRA-UTERINE LIFE. R. P. RANKEN LYLE, Obst. Tr. Edinburgh M. J. **33**:34 (Feb.) 1926.

The writer mentions the initiation of antenatal work by the Edinburgh Obstetrical Society, and the reduction in the maternal and infant mortality thereby. In the conservation of intra-uterine life, he advocates cesarean section as now advisable in difficult cases of pelvic contraction or in vomiting of pregnancy, and that the operation may be done repeatedly on the same mother, and that sterilization of the mother or mutilation of the fetus is not justifiable. Induction of abortion for any reason will soon become contrary to medical practice. Cesarean section in the first confinement will save many infant lives that were lost by placenta previa, and by prolapse of the cord. Eclampsia has been reduced to a minimum by prematernity work, and its high infant mortality and prematurity have been greatly reduced.

Breech, face and transverse presentations can now be converted into vertex positions. The infant mortality of breech cases is about 10 per cent.

Professor Lyle is an enthusiastic advocate of those obstetric procedures which give the infant the best chance for life and normality. He predicts the more common use of cesarean section, with the possibility of 100 per cent safety for mother and child.

NEFF, Kansas City, Mo.

CONTRIBUTION TO THE THEORY OF LITHOPEDIA. ELLA FASTENAU, Frankfurt. Ztschr. f. Path. **33**:200, 1925.

There are many theories to explain the origin of lithopedia: the fertilization of an aberrant ovum in the peritoneal cavity, with implantation on the peritoneal surface, which is rare; displacement of a tubal pregnancy, through rupture of the tube, and secondary implantation on the peritoneal surface; or they may be due to the protrusion of the products of conception through the ostium abdominale of the oviduct, into the peritoneal cavity, which is possible only when the primary implantation is near the fimbriated extremity of the tube. Such displacements usually result in the death of the embryo, but a few survive the ordeal for a few months and an almost negligible number go to term. Fully 50 per cent of embryos produced in this way are deformed. If the fetus dies before ossification of the skeleton has begun, it may be absorbed; if ossification has begun (after the third month of pregnancy) absorption is difficult or impossible and a retained fetus results. This may undergo maceration, "skeletonization" (maceration of soft parts only), mummification or calcification. The writer explains how these processes occur, the importance of infection and inflammation in the train of events, the rôle of the vernix caseosa as a matrix for calcification on the surface, etc. The case this author reports occurred in a woman of 76, who doubtless had carried the lithopedion for about thirty years. The latter is described at length, with excellent photographs. It was a "lithokelyphopedion," or one in which the calcification is confined to the membranes and does not involve the fetus, which is mummified within the shell thus formed. This fetus probably died during the seventh month of pregnancy and was so misshapen as to be scarcely recognizable as a human offspring. The author notes that this is the usual event in such cases, ascribing the deformity to lack of development rather than to distortion of a fully developed fetus.

FOOT, Cincinnati.

MECHANICS OF VOCAL CORD VIBRATION, AND OF SNORING. Proceedings of the German Otolaryngological Society, Part 2, Supplement. TONNDORF, Ztschr. f. Hals-, Nasen- u. Ohrenh. **12**:241 (Nov.) 1925.

A stream of liquid, air or gas passing through a tube and encountering a narrowed place increases in speed with corresponding loss of pressure, even to a minus pressure, causing a "sucking in" at the point of greatest constriction. The mathematical formula of this process is given. Illustrations of this principle are the steam injector and the atomizer. In the larynx, the same physical conditions are present, namely, the conical narrowing below the rima glottis. When the cords are in the position of phonation, the air stream first forces them apart, and as the narrowed stream passes through under increased speed but decreased pressure, the cords are sucked in together again, and the rapid repetition of this process produces sound. Elasticity of the cords is not necessary for mere sound, but functions in the production of pitch, modulation and clarity of tone.

The same explanation applies to snoring, which occurs when relaxation of the soft palate permits the inrushing air to suck it against the tongue if the mouth is open, or against the pharyngeal wall in nasal breathing when the passages are sufficiently narrowed.

The author demonstrates this by some simply constructed apparatus.

LEWY, Chicago.

Diseases of the New-Born

ICTERUS IN THE NEW-BORN. G. L. HALLEZ, Nourrisson **13**:297 (Sept.) 1925.

Hallez conducted experiments to show (1) the amount of bilirubin in the serum of the new-born, and (2) the resistance of the red blood cells to hypotonic solutions. In a series of thirty-one cases he found a marked cholemia, even in those infants which did not show visible jaundice. In the same cases, the examination of the red blood cells showed that some of the cells showed a lowered resistance, while others showed an increase above normal.

A clinical study was made in nineteen cases. The icterus usually appeared on the second or third day, and lasted from four to fifteen days. Twelve of the infants were born at term and six prematurely. In nine cases there was a certain amount of edema. Fourteen of the infants recovered, three died from congenital debility, one from erysipelas and one from congenital syphilis.

From his researches, Hallez believes that icterus of the new-born is due to two factors; first, a transient functional liver insufficiency with increased bile pigment in the serum, and second, an increased destruction of the red blood cells, with further liberation of bile pigment in the serum.

ICTERUS NEONATORUM. H. SLOBOSIANO AND P. HERSCOVICI, Nourrisson **13**:373 (Nov.) 1925.

Icteric infants show a greater initial weight loss, regain their birth weight more slowly, nurse poorly and are prone to digestive disturbances. This jaundice occurs more commonly in premature infants and lasts longer with them. Examination of the cord blood in all new-born infants shows an increase in the amount of bilirubin. The intensity of the icterus is not always an index of the concentration of bile pigment in the plasma. The authors believe the icterus is due to impaired excretory function of the liver, causing an abnormal accumulation of bile pigment in the blood. It has been claimed that cinchophen is able to increase the quantity of bile and to render it more acid. Proceeding from this

hypothesis, the authors decided to use it in cases of icterus neonatorum. The results were encouraging. Seventy-two subjects were treated, and of these 79 per cent had recovered when discharged from the hospital on the twelfth day. Of the fifty infants not treated, only 32 per cent had recovered by this time. An extensive bibliography is appended.

McClelland, Cleveland.

Singers' Nodes and Voice Disturbances. Proceedings of the German Otolaryngological Society, Part 2, Supplement. Sokolowski, Ztschr. f. Hals-, Nasen- u. Ohrenh. **12**:246 (Nov.) 1925.

This author does not agree with Flatau that nodes may be temporary disturbances, but believes there is always some pathologic substratum. Imhofer's statement that all his patients recovered by rest and local applications alone, is not corroborated by the author's experience. He believes that all subjects who do not respond to two or three months' rest should be operated on, and the use of the voice in singing "over" the difficulty results in permanent injury which cannot be restored by operation. Rest not only of the singing voice but also of conversational voice, is indicated; otherwise it is useless.

Lewy, Chicago.

Acute Infections

Auricular Endocarditis of Rheumatic Origin. W. C. Von Glahn, Am. J. Path. **2**:1, 1926.

From a study of nine cases, of which seven were children, the author concludes that there occur in the endocardium of the auricle, lesions which are distinctive both grossly and histologically, of rheumatic endocarditis. The endocardium of the left auricle is more frequently the site of the lesions than that of the right auricle. The lesions are described.

Cooke, St. Louis.

Renal Function in Scarlet Fever. G. H. Percival and C. P. Stewart, Edinburgh M. J. **33**:53 (Feb.) 1926.

These writers studied the urea content of the blood as a test of renal function in thirty-six cases of scarlet fever during the "nephritic period" of the disease. Of twenty-eight children, six developed nephritis. The author's technic was to examine the urine for the first ten days of the illness, so as to exclude preexisting nephritis, then to collect blood at the same hour during fasting intervals throughout the course. The urea was estimated by the urease method. The usual diet consisted of milk and cereals for twenty-one days, followed by addition of fish and white meat for the remainder. In case nephritis developed, the protein content of the diet was reduced.

The authors conclude that there is a moderate tendency toward high blood urea in the initial pyrexia, but more evident at the cessation of the fever. This is followed by a fall to the normal level. Then after the tenth day a second rise of urea occurs with or without clinical signs of nephritis. The characteristic difference in the urea of non-nephritic cases is the more rapid fall to normal, although one clinical case of nephritis had a decrease from 28 to 14 mg. of urea per hundred cubic centimeters of blood. In most of the nephritic cases, the second characteristic blood urea finding was the rise subsequent to the appearance of the clinical signs—oliguria, albuminuria, hematuria, casts and slight edema. They conclude that no warning of impending nephritis is given by blood

urea examination. Urea retention is to be considered a result of the nephritis. Transitory retention of nitrogen indicates a renal damage, which is too mild to give clinical symptoms.

NEFF, Kansas City, Mo.

CONGENITAL MEASLES. R. DEBRE, PIERRE JOANNON AND JOSEPH MARIANI, Nourrisson **13**:249 (July) 1925.

The authors believe that cases of congenital measles are much more common than a review of the reported cases would lead one to suspect. In fact, the natural immunity which some children seem to enjoy they believe can be explained in this way. They divide the cases into prenatal and postnatal. If the attack in the mother occurs before term and does not induce a premature labor, it is impossible to know whether the baby born later has had an intra-uterine attack of the disease or not. However, cases are reported by the writers in which it seems reasonable to suppose that such has been the case. One should also bear in mind the possibility of atypical manifestations in infants born prematurely during an attack of measles in the mother. Absence of a rash and Koplik spots does not prove the nonexistence of the infection in the debilitated infants who have too little vitality to react to the infecting virus. In the typical cases the authors have observed (1) fever, (2) a characteristic rash, which may consist only of a few macules, and (3) Koplik spots in three out of four cases. The coryza and conjunctivitis, however, are usually lacking. The authors believe that this can be explained by the transmission of the virus through the placenta and directly into the blood of the infant, rather than through the upper respiratory tract, the common portal of entry.

A case is reported in which the mother was exposed to measles and a day or two later was delivered of a normal child. Ten days after exposure, the catarrhal symptoms appeared in the mother, followed in a few days by the typical measles rash. In spite of a prophylactic injection of 3 cc. of convalescent serum given to the baby at this time, it developed Koplik spots three days after the appearance of the eruption in the mother and this was followed in a few days by the characteristic exanthem. The authors report this case to prove that the blood of the mother contained and transmitted the measles virus during the period of incubation.

In all cases of measles in the mother, the authors advise that the new-born infant should receive either prophylactic or therapeutic injections of protective serum.

McCLELLAND, Cleveland.

EPINEPHRIN IN DIPHTHERIA. J. MUNK, Jahrb. f. Kinderh. **108**:218, 1925.

The subcutaneous and intramuscular administration of epinephrin to diphtheria patients who showed symptoms of failing circulation raised the blood pressure to a marked degree, and in the author's opinion was a life saving measure in several instances cited. While the increase in blood pressure was greatest within the first half hour, it frequently remained at a definitely higher level than it had had prior to the administration of epinephrin for even as long a period as four hours. Thus, by repeating the medication four to six times a day, the patients could be carried through the period of imminent circulatory failure.

The cause of death from heart disease in diphtheria, the author believes, can be explained by the occurrence of an atonic condition of the blood vascular system, a fall of blood pressure and the consequent disturbed nutrition of the various

organs of the body, particularly of the vital centers in the central nervous system and finally of the heart itself.

The author also indulges in a discussion of the question why it is that, in some cases, diphtheria runs such a malignant course and in spite of serum treatment does not improve. That there may be several different strains of diphtheria bacilli, against some of which the antitoxin is not specific may be a factor but probably a very minor one. Undoubtedly, constitutional peculiarities on the part of the child are factors in some instances which must be considered. He concludes that by far the most important consideration is that sufficient serum be given at the earliest possible moment.

PARMELEE, Chicago.

OCCURRENCE OF OXYURIS VERMICULARIS IN SCHOOL CHILDREN. ARNOLD JAPHA, München. med. Wchnschr. **72**:473-474, 1925.

The author examined 200 children for ova of intestinal parasites, and found oxyuris 132 times, ascaris 3, taenia 3. Once he found a female oxyuris in the vulva of a girl with vulvitis. All 200 children had some symptoms which led him to suspect parasites. Afterward, he examined 285 children from one elementary school and found oxyuris ova in 209 cases, but no ova of taenia or ascarides. Older children were less frequently infected than the younger. He made only one examination, scratching the fecal material from the anal folds with a glass spatula and examining the material under a microscope. The author tried to get rid of the infection in a larger number of selected cases through purely hygienic measures, but with very little result. He believes in the possibility that parasites develop in the intestine.

THE OCCURRENCE OF DIPHTHERIA BACILLI IN THE WOUNDS OF HORSES. H. KLIEWE and M. WESTHUES, München. med. Wchnschr. **72**:587-589, 1925.

Bacteriologic examination was made of seventy wounds in horses at the hygienic institution of the University of Giessen, and it was found that twelve were infected with pathogenic diphtheria bacilli, two with pseudodiphtheria and five with paradiphtheria bacilli. The cultural and animal inoculation results are reported in detail. There is a probability that the so-called natural immunity to diphtheria in horses may be due to a past infection with diphtheria bacilli. Infection of man through contact with infected wounds and vice versa has not been demonstrated in the institution.

GROB, Rochester, Minn.

PATHOGENESIS OF DYSARTHRIA SPASTICA. Proceedings of the German Otolaryngological Society, Part 2, Supplement. H. STERN, Ztschr. f. Hals-, Nasen- u. Ohrenh. **12**:278 (Nov.) 1925.

This author claims many stutterers suffer from vagotonia, and describes many symptoms associated with speech disturbances, for instance, anomalies of respiration, that are due to increased vagotonic irritability. Although he recognizes the psychic element, he believes vagotonia to hold an important causal relationship, and that this relationship is of greatest importance in the course, prognosis and therapy. He will publish a more detailed article elsewhere.

LEWY, Chicago.

THE DETECTION OF THE BORDET-GENGOU BACILLI AND THEIR ETIOLOGIC SIGNIFICANCE FOR PERTUSSIS. W. BACHMANN and E. BURGHARD, Ztschr. f. Kinderh. **39**:465, 1925.

To separate the Bordet-Gengou bacilli from influenza bacilli is impossible. There is some ground for hope that the differentiation may be possible by the inoculation of mice, since mice infected with the pertussis bacilli nearly always die with bacteriemia.

No causal relation between the Bordet-Gengou bacilli and pertussis was found. No endotoxin action could be demonstrated, and intracutaneous inoculation as a means of diagnosis was unsuitable.

The authors, however, point out that their negative results do not speak against the etiologic significance of the Bordet-Gengou bacilli. On the other hand, the regular occurrence of these bacilli in the early stages of the sickness, the possibility of a bacteriologically early diagnosis, even before the outbreak of clinical symptoms, the marked virulence for mice, lead to the assumption that the bacilli are not merely accompanying bacilli of the disease but are to be looked on as of etiologic significance. The use of droplet plates in diagnosis and prophylaxis is warmly recommended.

EMERSON, Boston.

MEASLES PROPHYLAXIS. JAROSLAV PROCHAZKA, Cas. lek. cesk. **64**:100 (Jan.) 1925.

Of ninety cases immunized with convalescent serum, only five developed measles. Of these, three had serum from a single mild case. The other two developed measles on the thirty-third day following immunization, which may point to the shortness of the immunity. All five subjects had mild cases of measles. Koplik spots or a rash were the indication for immunization of contacts, with 2.5 cc. of a polyvalent serum obtained on the seventh to the ninth day following the return to normal temperature. The prophylaxis is especially recommended for very young infants, marantic or weak infants and children with any signs of tuberculosis.

STULIK, Chicago.

Chronic Infections

NUCLEAR INCLUSIONS IN THE TESTICLES OF MONKEYS INJECTED WITH THE TISSUE OF HUMAN VARICELLA LESIONS. THOMAS M. RIVERS, J. Exper. Med. **43**:275, 1926.

Eosin-staining nuclear inclusions in the epidermal cells and endothelial leukocytes are a most characteristic feature of the lesions of certain filterable virus diseases including chickenpox, herpes simplex and herpes zoster. In the experience of the author as well as some other workers, typical eosin-staining nuclear inclusions have never been found except in virus diseases.

When emulsified tissue of human varicella skin lesions was injected into the testicles of African vervets, histologic examination of the testicles, removed five and six days after inoculation, revealed eosin-staining nuclear inclusions in four animals. Nuclear inclusions were not found in the testicles of a vervet inoculated with normal skin.

MCCLURE, Evanston, Ill.

CONGENITAL SYPHILIS. H. LEMAIRE, Nourrisson **14**:18 (Jan.) 1926.

There being no primary lesion in congenital syphilis, the lesions encountered resemble the secondary and tertiary manifestations encountered in the adult, except that certain organs seem especially vulnerable in the infant; the epiphyses, glands, liver and spleen. The disease is often associated with such congenital malformations as harelip, spina bifida, meningocele, cardiopathies and certain encephalopathies. The septicemia type is particularly malignant; the other forms are usually benign. In the former, the best results are obtained with intravenous injections of neo-arsphenamine; the cutaneous lesions show marked improvement within forty-eight hours. Next to the arsenicals, bismuth seems to give the best results and is to be preferred to mercury. In cases of Parrot's pseudoparalysis, inunctions of mercury are recommended.

When visceral lesions are present, prolonged treatment is required. When the liver is involved, mercury is better tolerated than the arsenicals. With involvement of the central nervous system, intensive treatment with both mercury and arsphenamine is necessary. When arsenic is badly tolerated, bismuth should be used.

In all cases treatment should be carried out in regular prescribed courses till the child is 4 years old. Too much reliance should not be placed on the Wassermann reaction.

McCLELLAND, Cleveland.

PATHOLOGY OF KERATOSIS PHARYNGIS. Proceedings of the German Otolaryngological Society, Part 2, Supplement. ANTHON, Ztschr. f. Hals-, Nasen- u. Ohrenh. **12**:298 (Nov.) 1925.

This is essentially a cornification of the epithelium, not only of the crypts of the tonsils but of those of the entire Waldeyer's ring. The leptothrix is recognized as a constant accompaniment of this condition, but not in a causal relation, but rather as a secondary inhabitant. Therefore the names "mycosis tonsillaris" and "tonsillitis leptothrixia" are misnomers. A careful histologic and bacteriologic examination has been made, and the author believes he has shown that an encapsulated diplobacillus of the Friedlander type is a constant accompaniment. While the Koch cycle has not been completed, the author suspects a causal relationship, if not with the cornification at least he feels sure that the loss of luster of the pharyngeal mucosa in keratosis is due to the well known mucus producing effect of this diplobacillus.

LEWY, Chicago.

ON THE PROGNOSIS OF TUBERCULOSIS IN CHILDHOOD. E. NASSAU and H. ZWEIG, Ztschr. f. Kinderh. **39**:484, 1925.

The prognosis for a baby infected in the first three months of life is absolutely bad, and death occurs in the first half year. Eighty per cent of those infected in the first nine months, die. There is a relatively good prognosis for infants infected in the first year, who live through the second year. To attempt to make a prognosis for tuberculosis in later childhood is very difficult. It is unfavorable for pulmonary tuberculosis if it is a late infection; that is, after the sixth year, which is immediately followed by pulmonary disease. It is favorable if the pulmonary tuberculosis follows a transient letting down of the defences due to infectious diseases. It is favorable also if there was, long before, a latent tuberculous infection. Cases with recurrent phlyctenules seldom are followed by pulmonary tuberculosis.

EMERSON, Boston.

Internal Diseases

SPLENOMEGALY (TYPE GAUCHER) AND LIPOID HISTIOCYTOSIS (TYPE NIEMAN). WILLIAM BLOOM, Am. J. Path. **1**:595, 1925.

Two cases are reported, a boy aged 6 years, and a woman aged 42, in whom there was a history of long-standing increase in the size of the spleen, leukopenia, mild secondary anemia, and epistaxis in one case and uterine bleeding in the other.

Microscopically, there are large pale cells which contain iron and give no typical reactions with the usual lipoid stains in the spleen, liver and lymph nodes. These cells have a marked longitudinal striation with Mallory's aniline blue connective tissue method. These two cases seem to be typical of Gaucher's disease.

Three cases of the condition first described by Niemann are reported in infants aged 18, 14 and 7 months. The history in the first two of these was of long continued disturbance in feeding and a failure of the infants to develop. The third patient died of meningitis at a comparatively early period in the disease. In one patient the condition was recognized "in vivo," and improved a good deal for two months after splenectomy, but then began to fail again.

Anatomically, these cases have a widespread infiltration of lipoid material in the reticulum cells of the spleen, lymph nodes and thymus, Kupffer cells, clasmatocytes of connective tissue, and the large cells in the alveoli and perivascular tissues of the lung. The large foam cells are also present in the arteries of the lungs, pancreas and kidneys, and in the branches of the portal vein. In sharp contrast to the Gaucher cells, these cells stain positively for the complex lipoids, they do not contain iron and are markedly vacuolated after treatment with absolute alcohol. The absence of the large cells from blood smears can probably be explained on the basis of their being filtered out by the capillaries, especially those of the lungs.

A CASE OF RHEUMATIC AORTITIS WITH EARLY LESIONS IN THE MEDIA. A. M. PAPPENHEIMER and W. C. VON GLAHN, Am. J. Path. **2**:15, 1926.

The authors report a detailed histologic study of the aorta of a child aged 9 years, with rheumatic fever, in which changes of the media and adventitia accompanied typical valvular and myocardial rheumatic lesions. Their findings support the view that the perivascular medial scars are the sequel of an earlier focal perivascular inflammatory lesion.

COOKE, St. Louis.

ROENTGENOGRAPHY OF HYDATID CYSTS OF THE LUNG. CARLOS HEUSER, Am. J. Roentgenol. **13**:529 (June) 1925.

In Buenos Aires, cysts are seen with equal frequency in men, women and children; they are as frequently on the left as on the right and in any part of the lung; and they occur with equal frequency in the country and the city. Without the roentgenogram, diagnosis is almost impossible, and even with it, differentiation between pulmonary cyst and sarcoma in some cases is made only at operation. Roentgenographically, pulmonary cyst appears as a rounded shadow with clear cut borders, with the concavity toward the midline. If the border is rough and irregular the diagnosis of cyst must be doubted.

THE PRESENT STATUS OF THE ROENTGEN TREATMENT OF PURPURA HEMORRHAGICA BY IRRADIATION OF THE SPLEEN. HENRY K. PANCOAST, EUGENE P. PENDERGRASS and THOMAS FITZ-HUGH, JR., Am. J. Roentgenol. **13**:558 (June) 1925.

Stephan states that deep irradiation of the spleen produces a rapid decrease in the coagulation of blood in vitro, and has the same effect as an extensive loss of blood. The coagulation is shortened to one-fourth in normal persons. Some authors found in addition an increase in the platelet count after stimulating doses. These authors feel that roentgen action is destructive rather than stimulating, so far as the spleen is concerned. Of six cases treated with one-fifth of an erythema dose, five showed at least a temporary improvement. The hematologic picture of purpura hemorrhagica, thrombocytopenic purpura or essential thrombopenia is (1) reduced number of platelets in the circulating blood, (2) a concomitant lack of normal retractility of the clot, (3) a prolonged bleeding time, (4) a normal or only slightly delayed clotting time and (5) a positive tourniquet test for capillary resistance. Transfusion and splenectomy have a positive value in the treatment, and massive splenic irradiation may be of greater value. There is an extensive review of literature and a bibliography.

STULIK, Chicago.

CLINICAL CALORIMETRY. XXXIX. EXERCISE AND THE RESPIRATORY QUOTIENT IN DIABETES. HENRY B. RICHARDSON and SAMUEL Z. LEVINE, J. Biol. Chem. **66**:161, 1925.

A study was made of the respiratory quotients of normal and diabetic persons at rest and during exercise, which increased the total metabolism from 50 to 100 per cent. Whereas, in normal persons, exercise tended to cause an increase in the respiratory quotient, in diabetics the respiratory quotient was lowered. The authors believe that the lowered respiratory quotient indicates a decrease in the proportion of carbohydrate katabolized in the body. They do not believe that fat is converted to carbohydrate in the course of its metabolism.

HIGGINS, Cincinnati.

A STUDY OF THE MECHANISM OF INSULIN. THE ACTION OF INSULIN AND OF THE SALTS OF GUANADINE ON THE PERMEABILITY OF THE MAMMALIAN ERYTHROCYTE. J. SECHER, J. Physiol. **60**:286-292, 1925.

Quantitative chemical and microscopic evidence is given in support of the view that the mechanism of insulin is to increase the permeability of the cell membrane. Guanidine behaves like insulin in this respect, and the presence of calcions is essential for this action.

KUGELMASS, New York.

PROGRESSIVE ARTERIAL CHANGES IN HYDRONEPHROSIS. DUNCAN M. MORRISON, Tr. Edinburgh M. J. **33**:14 (Jan.) 1926.

The writer reports the attempt to find the mechanism of hydronephrosis which is particularly complex and as yet not known. He injected the renal blood vessels of rabbits with barium gelatin in some cases, and a celluloid corrosive in others. These methods show the great vascularity of the kidney, and that the arteriae rectae come from the efferent vessels of the malpighian tufts. He summarized the arterial changes leading up to total experimental hydronephrosis. The medulla of the kidney is compressed by the distention of

the pelvis and the arteries become progressively short and tortuous. The cortex shares in the pressure, and the peripheral glomeruli undergo atrophy, with changes in the interlobular arteries and their final disappearance. The ureter becomes totally obstructed and the kidney is transformed into a thin-walled sac, with no blood vessels remaining except the vascular trunks which course over and around the sac. The writer concludes that circulatory conditions play an important part in hydronephrosis.

In the discussion which followed, Professor Russell said that this interesting study of the stages of nephrosis does not explain the tendency to suppuration, which he has seen in young persons. He once saw a boy aged 12 years, with hydronephrosis of congenital origin. It was found at operation that an aberrant artery crossed the ureter at the middle of its course. This was ligated but without relief of the kidney swelling, which was intermittent and had been erroneously considered to be recurrent colonic obstruction. Professor Russell concluded that in this case the lower end of the ureter had not developed properly because of the early pressure by the artery, and that it could not drain off excessive amounts of urine except slowly. The pelvis became infected and the kidney later had to be removed.

A Case of Fibroid Lung. Charles McNeil, Tr. Edinburgh M. J. **33**:33 (Feb.) 1926.

A boy, aged 7 years, with fibroid lung and displacement of the heart and trachea to the right, has been followed for six and one-half years. There had been extensive disease of the right lung and pleura, shown clearly in the roentgenogram. The contracted right lung is drawn over the heart. The lateral position of the trachea can be felt above the sternum. The disease began with measles and pneumonia at the age of 5 months, but has not interfered with his later health. There is no cyanosis nor clubbing of the fingers.

Neff, Kansas City, Mo.

Pyloric Stenosis. A. Morlet, Nourrisson **13**:245 (July) 1925.

When there is a partial stenosis of the pylorus, greater muscular force is required to force food through the narrowed opening. This results, according to the author, in a compensatory hypertrophy of the circular muscle fibers of the stomach. Finally the muscles of the pylorus itself are involved, and this tends to a still further narrowing of the lumen, esepcially when there is a spasm of these muscle fibers. This also explains why these subjects often have a free interval of several weeks before the vomiting becomes excessive. It also explains the benefit obtained by the Fredet operation. In cutting the circular fibers of the pylorus, the lumen is enlarged and the constricting effect of the circular fiber is destroyed.

McClelland, Cleveland.

Goiter Prophylaxis in School Children. A. Eckstein and O. Feldmann, Arch. f. Kinderh. **75**:263 (March 20) 1925.

The goiters were divided into three classes according to size: class 1 being made up of thyroids which were definitely palpable but not visible; class 2 being slightly larger glands, visible in profile; and class 3 consisting of the large goiter whose size overshadowed the other structures in the neck. Of 4,800 school children in Freiburg, thyroid enlargement was present in 86 per cent of the boys and 95 per cent of the girls, even in the first school years, the size growing larger as the age advanced. The latter was especially striking in the girls near the age of

puberty, in whom the nodular type of goiter was also more common than in the boys. Tablets containing 1 mg., or in some cases, 3 mg., of iodine were given once a week to 485 children, of whom 333 were followed for longer periods of time, up to one and one-half years. Among the children with class 1 goiter, successful results (decrease in neck circumference by at least 2 cm.) were obtained in about one-quarter of the cases, in class 2, 49 per cent, and in class 3, 65 per cent. The larger the goiter, the more successful the result, and there was no demonstrable difference in effect whether 1 or 3 mg. of iodine were given. Treatment should be continued for two months, then interrupted. No harmful effects from the iodine were observed, although other reports dealing with a larger material have stated that an increase in the number of cases of hyperthyroidism may occur.

HEMPELMANN, St. Louis.

THE TREATMENT OF PYLOROSPASM. F. HAMBURGER, München med. Wchnschr. **72**:302-303, 1925.

One case is mentioned, in which 0.1 mg. of atropine subcutaneously gave a very good result. The same infant, who was 5 months old and weighed 3,500 gm., was given 1.8 mg. of atropine by mouth with no result as to vomiting nor as to action on the pupils. Ritte, of Graz, found that usually not more than about one and a half to twice as much atropine is necessary on oral as on subcutaneous administration. It was surprising to find that it takes from 15 to 120 times the dose of novatropine administered by mouth.

GROB, Rochester, Minn.

THE CAUSE OF TONSILLOLITHS. Proceedings of the German Otolaryngological Society, Part 2, Supplement. EHRENFRIED, Ztschr. f. Hals-, Nasen- u. Ohrenh. **12**:327 (Nov.) 1925.

Tonsilloliths are formed of calcium phosphate, while salivary stones and tooth stones are calcium carbonate. Ehrenfried found fungi on freshly removed tonsilloliths, and believes that fungi, because of their attraction for lime salts, may play an important rôle in causation.

LEWY, Chicago.

ROENTGEN CONTROL OF THE D'ESPINE SIGN. F. SKALNIK, Cas. lek. cesk. **64**:213 (Feb.) 1925.

The author studied fifty-three cases, and found that bronchophony may be heard over pathologically increased areas in subjects showing no hilum changes roentgenologically, as well as in those having definite hilum changes. Likewise, the D'Espine sign may be negative in subjects having definite hilum changes. The D'Espine sign cannot, therefore, replace the roentgenogram in the diagnosis of hilum gland changes.

STULIK, Chicago.

Nervous Diseases

A CASE OF CEREBELLOPONTILE ANGLE TUMOR WITH EXAMINATION OF THE VESTIBULAR APPARATUS, AUTOPSY. FRANK DENNIS, Ann. Otol. Rhin. & Laryng. **33**:863 (Sept.) 1924.

Dennis states that Jones and Fisher have pointed out that the responses to stimulation of the vestibular apparatus are more characteristic in lesions of the cerebellopontile angle than in other intracranial lesions. The syndrome is: complete deafness on the side of the lesion, lack of responses to stimula-

tion of the vertical semicircular canals of both sides, with good responses from the contralateral horizontal canals. The patient, aged 16, whose case is presented showed signs of brain stem lesion: spontaneous vertical nystagmus upward, staggering, right facial nerve paralysis and bilateral choked disk with beginning atrophy on the right. The physical examination revealed: failing hearing and tinnitus; diplopia corrected by glasses; headache; vomiting, projectile in character; failing vision and staggering spells of blindness; difficulty in swallowing, but no choking; less of control of the muscles of the back, and pain and spasm of the right leg and hip. The neurologic examination revealed: a right facial paralysis; the tongue protruded on the midline with tremor; the reflexes were diminished on the right; there were no Gordon, Oppenheim, Chaddock or Babinski sign; the joint and stereognostic sense was normal. The finger to nose test showed incoordination with both arms. The patient walked with feet apart and lifted the right foot high and in a spastic manner. Bilateral choked disk was present and there was beginning atrophy on the right. The neurologic diagnosis was: right angle tumor. Otologic examination of the ear, nose and throat showed nothing abnormal. A hearing test disclosed deafness of the right ear and a slight degree of obstruction deafness in the left ear.

Vestibular tests: spontaneous, horizontal nystagmus to the right and left on looking right and left; vertical nystagmus upward; crossed past pointing, in the right hand 4 inches (10 cm.) to the left, in the left hand 4 inches to the right. The Romberg test caused marked swaying. Douching at 168 F. of the right ear caused no nystagmus with horizontal or vertical canal and no past pointing with the right arm, but past pointing of 8 inches (20 cm.) to the right with the left arm. Douching of the left ear caused no nystagmus from the left vertical canal; past pointing of 4 inches to the left with the right hand occurred with stimulation of the verticals, and with both hands to the left when the horizontal canal was stimulated. The diagnosis made was: cerebellopontile angle lesion of the right side.

A suboccipital exploration was undertaken and the dura exposed; bulging of the cerebellum was noted, more marked on the right; resistance was also increased on the right, but no tumor was found. The patient died. At necropsy, the skull cap was thin in the parietal region, especially on the right side. The convolutions were flattened, and there was marked increase of fluid in the ventricles. After the brain was removed, a firm smooth tumor, 6.5 by 7.5 cm., was found at the right cerebellopontile angle. The right cerebellar hemisphere was pushed to the left and backward, and the brain stem was displaced to the left. The right acoustic nerve entered the tumor. No adhesions were found between the tumor and the cerebellum. A histologic diagnosis of neurofibroma was made.

Tumors of the acoustic nerve are small. This emphasizes the need for more frequent application of vestibular tests in ear cases, particularly those showing tinnitus and deafness. If this patient could have been examined sooner, vestibular signs of beginning intracranial involvement would have been found, and an examination would have completed the diagnosis by revealing characteristic phenomena of intracranial pressure due to a definite lesion.

FAY, Philadelphia.

ATYPICAL AND MASKED FORMS OF ENCEPHALITIS. AXEL V. NEEL, J. Nerv. & Ment. Dis. **63**:1 (Jan.) 1926.

The author seeks to find certain pathologic changes in the spinal fluid in indistinct and atypical cases of encephalitis which have been diagnosed otherwise. He discovered that after 1921 certain changes in the spinal fluid occurred more frequently than before—very slight increase of albumin with or without a very slight increase of cells. Reports on spinal fluids of such cases between the years 1916 and 1921 were reexamined, and the presence of these findings confirmed the author's assumption that epidemic encephalitis occurred in Copenhagen during the years immediately preceding the announcement of the epidemics in Australia, France, Vienna and England. Of the 125 cases studied, pathologic changes were found in all but two cases, contradicting statements that spinal fluids in encephalitis show nothing abnormal. One case is reported of typical acute epidemic encephalitis resulting in death in which the spinal fluid appeared to be normal. Microscopic examinations revealed the following changes: pronounced round cell infiltration around vessels, most noticeable in the central ganglia, cerebral trunk and cerebellum; pigment cells and small hemorrhages, perivascular in distribution, together with hyaline and other alterations in the vessel wall leading in some instances to obliteration. The vessel endothelium sometimes showed sufficient proliferation to produce this result. These changes were pronounced in sites usually affected by encephalitis in addition to the usual microscopic findings of encephalitis.

HART, Philadelphia.

THE PATHOGENESIS AND TREATMENT OF TETANY IN INFANTS. ALVIS BRATUSCH-MARRAIN, Arch. f. Kinderh. **75**:255 (Feb.-March) 1925.

After reviewing certain parts of the literature dealing with the clinical effects of various diets on infants with tetany, the writer gives his own impressions. Tetany can always be promptly and favorably influenced by withdrawal of the milk in the diet. The milk free diet, however, if long continued, leads to disturbance of nutrition. Wernstedt's milk mixtures with very high carbohydrate content also cause definite, though often slight, improvement probably because of the production of acids from the sugar fermentation. The high percentage of carbohydrate, however, is apt to cause diarrhea. The administration of ammonium chloride (four cases) and hydrochloric acid milk (three cases) seemed to produce definite if only temporary benefit, although the cases are too few to draw accurate conclusions. Calcium, in the form of calcium lactate, was slower in action than the last two remedies, but seemed to have a more lasting effect. The best treatment would appear to be withdrawal of milk, and, if necessary, the administration of ammonium chloride, calcium, and phosphorus with cod liver oil.

HEMPELMANN, St. Louis.

LA DÉGÉNÉRESCENCE HÉPATO-LENTICULAIRE. ÉTUDE CLINIQUE, ANATOMIQUE ET EXPÉRIMENTALE (CONTINUED). IVAN MAHAIM, Schweiz. Arch. f. Neurol. u. Psychiat. **17**:43-62, 1925.

Mahaim continues his discussion by reporting the case of a boy, aged 9, free from hereditary abnormalities, and a brother of 5, both in good health. About two years before, he was hospitalized because of mental deficiency and misbehavior. Up to this time his mental attainments were normal and he was at the head of his class. He had suffered a fracture of the thigh a few

months before, after which he spoke less frequently, cried easily and exhibited a slight tremor. On examination, his handwriting was found to be tremulous, he did not speak spontaneously, his emotional reactions were fickle, the reflexes were active and on movement there was a generalized hypertonicity. He was discharged with a diagnosis of imbecility. One month before death he was readmitted, at which time he was emaciated and dysphagic, and exhibited a marked generalized hypertonicity and extremely slow and athetosic movements. The reflexes were difficult to elicit; the Babinski phenomenon was negative; no tremor was noted. He became steadily worse, developed a hyperpyrexia and died.

Necropsy disclosed a marked atrophic cirrhosis of the liver, many newly formed bile passages and proliferation of connective tissue with formation of nodules throughout. The hepatic cells did not appear to be altered. The cerebral lesions were limited almost entirely to the striate body. A bilateral lacunar condition involved the greater part of the globus pallidus; hemorrhagic lesions were noted in the putamen which appeared to be reduced in volume. The cerebral cortex showed some discrete alteration of the ganglion cells and a slight generalized proliferation of the glial elements. The hypertonicity with athetosis and spasmodic contortions were attributed to the pallidal involvement.

Jakob reported a detailed study of extrapyramidal motor disturbances. In Huntington's chorea the striatum and the cerebral cortex were found to be involved. Two cases of paralysis agitans complicated by unilateral athetosis were reported by him. Necropsy disclosed diffuse lesions of the striatum and pallidum and a necrotic area in the pallidum opposite the athetosic side. According to him, athetosis only appears if the pallidum is markedly involved. In congenital double athetosis the situation is more complicated and the pathogenesis cannot be reduced to a single constant lesion. Recently Wimmer reported a case of pseudosclerosis without hepatic cirrhosis; however, this case does not withstand scrutiny for it resembled Friedreich's paramyoclonus, and it is difficult to form a satisfactory opinion of the exact pathologic changes found from his description. A similar criticism applies to cases of torsion spasm without hepatic cirrhosis reported by Richter, Cassirer and Westphal.

The parallelism of hepatolenticular degenerations remains a mystery. Wilson regards the hepatic degeneration as primary. The liver, he believes, produces a toxin which acts in a deleterious manner on certain portions of the brain. He is of the opinion that the affection is acquired in spite of the fact that it appears to be familial. Other writers lay more stress on the familial characteristics of this malady. Some believe that the liver and brain changes develop simultaneously as the result of a common noxious agent. One of the curious features of the hepatic cirrhosis is that it produces no clinical signs. Occasionally a slight icterus may be noted.

Mahaim undertook some experimental work to see whether he could produce hepatic cirrhosis by introducing a toxic substance into the biliary passages. He found on preliminary injection with methylene blue in a rabbit or dog that the biliary passages may be infiltrated to the finest ramifications. He next introduced 50 per cent ethyl alcohol through a biliary fistula formed by suturing the gallbladder to the abdominal wall. The liver of a dog so treated showed a marked generalized biliary pigmentation, necrosis and connective tissue reaction. *(To be continued.)*

WOLTMAN, Rochester, Minn.

ELECTRIC INITIATION OF THE VAGI IN MAN. E. STAHNKE and SEYERLEIN, München. med. Wchnschr. **72**:334-335, 1925.

Electrodes were brought into the esophagus with a sound. The results were almost identical with those in dogs, with direct stimulation of the vagi. A weak stimulation showed itself in the stomach by an increased tonus, increased peristalsis, deeper and more numerous. A moderate stimulation caused very deep waves, the stomach often seemed as if it were divided into three parts. The descending part of the duodenum contracted, giving the impression of antiperistalsis. The contrast meal returned from the bulbus to the stomach. With strong stimulation, peristalsis of the stomach was, if possible, even more definite. The pylorus kept open and the bulb did not empty itself any longer. The pylorus was opened and closed by the vagus, according to the degree of stimulation. The bulbus duodeni, with regard to function, is a unit with the stomach and is governed by the vagus.

THE SYMPTOMATOLGY OF THE TETANY OF INFANTS. A. BRATUSCH-MARRAIN, München. med. Wchnschr. **72**:593, 1925.

In a short article, the author gives the history of an infant with tetany who responded with a contraction of the muscle if the middle of M. biceps brachialis or M. quadriceps femoris was hit. Petényi described this symptom recently, and called it quadriceps phenomenon.

GROB, Rochester, Minn.

PAPILLARY CARCINOMA OF THE CHOROID PLEXUS OF THE FOURTH VENTRICLE. G. TÖPPICH, Frankfurt. Ztschr. f. Path. **33**:238, 1925.

Töppich first points out the salient differences between the histology of the epithelium of the choroid plexus and that of the ependyma of the ventricles: the former is cuboidal, nonciliated (although ciliated during fetal life) and has a squared-off base, without any basilar processes; the ependymal cell is cylindric, but is often ciliated in adult life and possesses a branched basilar process of neuroglia, demonstrable with the proper technic. Under conditions of neoplasia, however, the plexus epithelium may be cylindric, with rounded and smooth outer margin, but having no basilar process; the difference between these two types of cell now becomes very difficult to recognize. He says that it has been neglected and that few reports give reliable data on which one could base a diagnosis of the origin of the tumors they describe.

Having academically stated his thesis, the author describes a case of papillary carcinoma of the choroid plexus in a child of 2 years. There was flaccid paralysis, moderate atrophy of both legs, no sensation from slightly below the umbilical level to the lower limit of the distribution of the tenth and eleventh dorsal segments, incontinence of urine and feces, decubiti and trophic skin lesions. The history extended over the last three months of the child's life. On the day of death, the child had several cramp-like convulsions of the back and neck with unconsciousness, lasting about two minutes each time. Lumbar puncture showed many fat-granule cells, erythrocytes, but no tumor cells. The clinical diagnosis was transverse myelitis.

Necropsy revealed a tumor of the choroid plexus in the fourth ventricle. It was the size of a plum and involved the plexus so thoroughly as to obliterate its architecture; it had metastasized all along the cord, doubtless by way of the

cerebrospinal fluid, to the cauda equina. It was composed of masses of cylindric cells, without cilia or basal processes, arranged in papillary projections and sheets over the surface of a connective tissue stroma. Sometimes the epithelium was cuboidal and formed a single layer. A photomicrograph of the tumor accompanies the article.

FOOT, Cincinnati.

BORDIER TREATMENT OF ACUTE PALSIES OF CHILDHOOD. J. SVEJCAR and F. DREUSCHUH, Cas. lek. cesk. **64**:20 (Jan.) 1925.

Because of the tendency to heal, it is difficult to estimate the value of roentgen therapy, especially as serum, diathermy, hot baths and galvanization are used coincidently. Roentgen therapy should be instituted as soon as there is a tendency to improve. In the reviewed cases and the author's case, the results were promising. The action is regarded as stimulating to both nerve and muscle elements.

STULIK, Chicago.

Diseases of the Eye

SOME ESSENTIALS OF GLIOMA OF THE RETINA. C. W. RUTHERFORD, Am. J. Ophthal. **9**:171, 1926.

The parents noted a peculiar appearance in the right pupil in a child, aged 3½ months. General examination and history were negative The right eye was blind. The pupil was larger and reacted more sluggishly than the left. Behind the right lens was a yellowish rounded mass occupying the entire vitreous chamber. The diagnosis of glioma of the retina being made, the eye was enucleated and sectioned. The microscope revealed all the essential characteristics of a glioma of the retina.

V. WESCOTT, Chicago.

PATHOLOGICO-ANATOMIC FINDINGS IN CLINICAL LACUNAR TONSILLITIS. Proceedings of the German Otolaryngological Society, Part 2, Supplement. B. GROSSMANN and R. WALDAPFEL, Ztschr. f. Hals-, Nasen- u. Ohrenh. **12**:323 (Nov.) 1925.

In sections of tonsils removed during the acute attack of lacunar tonsillitis investigators show that the inflammatory process is not limited to the cryptic region, but that the infiltration and destructive process associated with streptococci and gram-positive diplococci extend throughout the tonsil tissues. (Incidentally, the subjects suffered no ill effects from tonsil removal during the acute attack.)

LEWY, Chicago.

EXTENSIVE TUBERCULOSIS OF AN EYE IN AN INFANT. T. M. LI, China M. J. **39**:1002, 1925.

The right eye of an infant, aged 10 months, was enucleated because of extensive tuberculous involvement, secondary to pulmonary tuberculosis. Tubercle bacilli were found in abundance. Search of the literature fails to reveal a report of a case with such extensive tuberculous involvement in an infant so young.

PILCHER, Cleveland.

Diseases of the Ear, Nose and Throat

CONGENITAL ATRESIA OF EXTERNAL AUDITORY MEATUS. LEO DEUTSCH, Monatschr. f. Ohrenh. **9**:993 (Sept.) 1925.

Roentgenographic examination of seven cases of bilateral malformation of the auricula and external canal prompts the author to divide his findings into two groups. The first shows a hypoplasia of the os tympanicum and a compensatory hyperplasia of the surrounding structures, especially of the processus styloideus and the mastoid. Their enlargement is at the expense of the malformed tympanic bone. In the second group the atresia results from a concentric narrowing of the canal. The annulus tympanicus enlarges by bone deposition on its external circumference and by bone resorption in the internal lumen. If this ontogenetic sequence is disturbed, resorption may cease and result in the narrow constricted external canal.

ENDONASAL GIANT CELL SARCOMA. GEZA KALOCSAY, Monatschr. f. Ohrenh. **9**:1031 (Sept.) 1925.

In 1900, Kümmel collected seventy cases of nasal sarcoma, and in 1902, forty more were added by Gibb. Among all these only two giant cell sarcomas (Nelaton, Mason) were found. The author's patient, a girl, aged 7 years, presented a tumor of the left ethmoid, encroaching somewhat on the orbital cavity and producing exophthalmos and ulcus corneae and lagophthalmos. Thirteen roentgen-ray exposures were made, entirely shrinking the tumor mass. A suppurating fistula near the internal canthus was the indication for a radical external ethmoid operation. The patient could not be followed further.

GLOWACKI, Detroit.

INSULIN IN OTOLARYNGOLOGY. Proceedings of the German Otolaryngological Society, Part 2, Supplement. SPIES, Ztschr. f. Hals-, Nasen- u. Ohrenh. **12**:334 (Nov.) 1925.

Spies uses insulin in so-called dry types of catarrh, even in ozena and pachydermia laryngis. Patients are first examined to make sure that blood sugar is up to normal (not under 0.08), and are given high carbohydrate diets, plus additional sugar several days before 3 to 5 units of insulin are used hypodermically daily or at longer intervals. Ampules of glucose solution for intravenous use are kept at hand, as is epinephrin and calcium preparations, but this investigator has not had any case of severe hypoglycemia.

LEWY, Chicago.

CLINICAL PICTURE AND THERAPEUSIS OF ACUTE TRACHEOBRONCHIAL FOREIGN BODIES. B. WISKOVSKY, Cas. lek. cesk. **64**:1-56 (Jan.) 1925.

The prebronchoscopy death rate of 52 per cent for foreign body inhalation has been cut to 8 per cent, with a low individual rate of 2 per cent credited to Jackson. Of the ten cases reported, two of the bodies were in the larynx; two were freely movable in the trachea and six were in the bronchi. Eighty per cent were in children. Because of bronchial relaxation, relatively large bodies are carried down. The author points to the dangerous habit of holding foreign bodies in the mouth and the use of bones during teething. The only treatment is removal with the bronchoscope. Great stress is placed on the history of foreign body aspiration. Roentgenograms are important in diagnosis, as definite symptoms may not appear early, because of mild reaction as

in the aspiration of smooth, sterile objects. The roentgenogram points are unilateral fixation of the diaphragm, decreased localized aeration, with compensatory emphysema and pulling of the mediastinum toward the affected side. At times, an emphysema may occur on the side of the plugged bronchus. Roentgenograms and pictures of the objects removed are presented. There is a bibliography.

STULIK, Chicago.

Diseases of the Skin

SO-CALLED ACRODYNIA OR ERYTHREDEMA (SWIFT'S DISEASE). S. B. WOLBACH and P. R. HOWE, Arch. Path. **1**:64 (Jan.) 1926.

Two clinically typical cases of "acrodynia" or "erythredema" which came to necropsy are reported by Warthin. The essential pathologic changes in these two cases were: extreme edema and slight meningeal irritation of the central nervous system, chronic erythema of the skin with hyperkeratosis, hypertrophy of the epidermis and sweat glands, with slight pigmentation of the rete, occurring in children of the hypoplastic lymphatic constitution, with associated or terminal respiratory infections and gastro-intestinal catarrh and inanition. These two cases do not support the theory of a polyneuritis as the essential feature of the disease; neither do they justify the use of the term "erythredema" as a fitting designation, as they showed no edema of the corium. They do not present any evidence as to a specific infectious etiology; they likewise show no relationship between tonsillar disease and the syndrome. *The changes in the skin and central nervous system suggested the pathologic change of the early erythema stage of pellagra.* The changes in the skin are also identical with those seen in certain forms of light sensitization xeroderma and fagopyrism. They are also identical with certain stages of roentgen ray and ultraviolet ray erythemas. The entire anatomic picture in these two cases suggests either a food deficiency or a toxic state action on persons of the hypoplastic constitution, affecting the reticulo-endothelial system of meninges and skin, the vegetative nervous system and possibly leading to a light sensitization.

[J. A. M. A.]

A SIMPLE TREATMENT FOR CUTANEOUS PAPILLOMA. N. R. HOUSTON, Edinburgh M. J. **33**:31 (Jan.) 1926.

The writer reports the treatment of sixteen cases of warts on the hands, mostly of children, with 1 per cent of liquor arsenicalis. This is swabbed lightly over the growth three times daily, until pain or inflammation necessitates discontinuance for a few days, and then once or twice a day until the wart disappears or the pain returns. The results are universally gratifying, and produce a minimum of scar tissue, less than if the common acids or alkalis are used.

A CASE OF NEVUS UNIUS LATERIS. CHARLES MCNEIL, Tr. Edinburgh M. J. **33**:32 (Feb.) 1926.

A girl, aged 7 years, showed a congenital nevus of extensive but unilateral distribution, on large areas of the trunk, leg and arm. The growth grew actively after an attack of measles at the age of 6, forming large pedunculated nevoid masses, accompanied by ulceration and bleeding. Some of the surfaces are scaly and hard. On the leg there is an overgrowth of hair. The nevus affects both

the skin and the subcutaneous tissues. Other mixed characteristics are involvement of the capillaries, the horny layer, the layer of pigment cells and the hairy elements.

NEFF, Kansas City, Mo.

THE REACTION OF THE SKIN OF PERSONS HAVING ECZEMA TO COCCI AND THEIR TOXINS. F. M. PETER, Dermat. Wchnschr. **80**:502 (April 4) 1926.

The author attempted to demonstrate the hypersensitization of the skin of patients having eczema by placing on areas of normal skin cocci (and their toxins) recovered from these eczemas. *Staphylococcus pyogenes-albus* was the strain usually recovered from the eczematous vesicles. Control patients, that is, patients having some other disease than eczema, were used. The author concluded that an artificial dermatitis can be evoked on the normal skin of persons with eczema by placing on that normal skin cocci or their toxins originally recovered from the same patient. The toxins produced the stronger reactions. He explained this by the production of allergy and secondary sensitization of the skin. No reaction was obtained on the controls.

[ARCH. DERM.]

A CLINICAL AND HISTOLOGIC STUDY OF AN UNUSUAL CASE OF THE JUVENILE FORM OF ACANTHOSIS NIGRICANS RESULTING IN BENIGN FIBROMATOSIS. HODARA and BEHDJET (LEVIN), Dermat. Wchnschr. **80**:609 (April 25) 1925.

The disease began at the age of 3, involving chiefly, the umbilicus, anal and perianal regions, the buttocks and back. Three years later, six large, soft, benign but deeply situated fibromas developed on the acanthosis lesions. In the next sixteen years the tumors were operated on twice, but the original six tumors recurred. No lenticular spots or melanodermas were ever present, but on the skin covering the summit of the tumors there is an occasional patch of acanthosis nigricans. These plaques under the microscope show the typical changes of acanthosis nigricans hyperpigmentation of the rete cells and a papillomatous proliferation of the corium. The tumor tissue itself is of a coarse fibrous nature, very poor in cellular elements, and is seen to arise from beneath the corium. The tumor never penetrates the cutis proper, and there is no tendency to pedicle formation. Numerous large comedones are found in certain regions of the skin covering the tumors.

McCARTHY, Washington, D. C.

THE REINJECTION OF OWN BLOOD. N. EBERS, München. med. Wchnschr. **72**:565-566, 1925.

To patients afflicted with furunculosis, impetigo contagiosa, chronic eczema, herpes zoster and labialis, the author reinjected their own blood. He used from 6 to 60 cc. of blood, injecting around or below the skin lesion. With the exception of one, all furuncles, ten in number, so treated healed in a very short time without leaving a scar. In impetigo contagiosa and chronic eczema, there was a good local response. Herpes zoster and labialis did not respond to this treatment. Some of the treated furuncles occurred on the basis of general furunculosis and the general furunculosis was not influenced.

GROB, Rochester, Minn.

CONTRIBUTION TO THE PHYSIOLOGY AND PATHOLOGY OF THE RESPIRATORY MUCOSA. Proceedings of the German Otolaryngological Society, Part 2, Supplement. H. STERNBERG, Ztschr. f. Hals-, Nasen- u. Ohrenh. **12**:340 (Nov.) 1925.

Vasomotor changes of the nasal mucosa following mechanical, nervous and pharmacologic stimuli:

1. Compression of the neck veins dilates nasal mucosa vessels; clamping the common carotid causes temporary loss of volume, soon regulated by collateral circulation.

2. Sudden noises and pain cause constriction of vessels. Deep narcosis causes vasodilation. Irritation of the uterus and chilling the caudal extremity caused no definite changes.

3. Laryngeal reflexes influence alae nasi movements and cause hyperemia of nasal mucosa.

4. Only constrictor impulses are elicited by neck stimuli. The vidian nerve carries principally dilator impulses, but to a small extent constrictor impulses.

5. Cold irrigation of the ear causes constriction; hot irrigation causes dilatation.

6. Intravenous injection of preparations of the suprarenal and the hypophysis causes high grade constriction with loss of pulsation. Histamin caused dilatation of vessels by decreasing venous outflow. Barbital-sodium was constricting. Other drugs dilate.

7. Cocain paralyzes dilators and leaves constrictors to work without opposition. This explains its well known local constricting action.

LEWY, Chicago.

SYSTEMATIZED FORMATION OF NEVI IN A HOMOLOGOUS PAIR OF TWINS. A CONTRIBUTION TO THE ETIOLOGY OF NEVI. M. BARDACH, Ztschr. f. Kinderh. **39**:542, 1925.

This author reports a bilateral systematized nevus depigmentosa which occurred equally in both of a pair of homologous twins, in the same general fashion, at the same time. This is considered evidence for the view of Levens, that twins from one ovum are not completely identical.

THE USE OF RESORCIN AND ITS HARMFUL EFFECTS IN CHILDREN. O. CONNERTH. Ztschr. f. Kinderh. **39**:628, 1925.

A fatal case is reported of an atrophic baby, aged 1½ years, treated for severe eczema, with a 5 per cent resorcin paste, for about fifteen days. Methemoglobin was demonstrated in the blood. This form of treatment is dangerous in babies in the first four months and in atrophic cases. The most promising therapeutic agent in this form of poisoning is exsanguination transfusion.

EMERSON, Boston.

Surgery and Orthopedics

HYPERTHYROIDISM IN CHILDREN. R. S. DINSMORE, Surg., Gynec. & Obst. **42**:172 (Feb.) 1926.

The incidence of hyperthyroidism in children is probably much higher than the published reports seem to indicate. After reviewing the entire American and foreign literature, Buford was able to find reports of only eight subjects under 5 years of age, and eighteen under 12 years of age. In a large series, Klein could gather only 154 subjects under 15 years. In the author's collection of forty-six cases, one was 5½ years old, one was 7 years, two were 8 years, two were 9 years, three were 10 years, four were 11 years, three were 12 years, thirteen were 13 years, and seventeen were 14 years of age. The cause of this condition is not easy to determine. In some cases there seems to be a family tendency toward hyperthyroidism, in some it is preceded by an acute infection involving the nose, throat or sinuses, and occasionally it is precipitated by too large a dose of iodine given as prophylactic measure.

The onset is ordinarily quite abrupt, being ushered in with nervousness, which is followed by enlargement of the gland, tachycardia and exophthalmus. Sometimes a tremor is seen and occasionally loss of weight is very rapid. As to the changes on the metabolic rate, there has been considerable dispute, because authorities have not as yet come to an agreement on the normal rate in the preadolescent period of life.

The management differs only little from that used with adults, but it must be kept in mind that children have to be very carefully handled, because the reactions to stimuli may be very severe. When foci of infection are present, it is safer to perform a thyroidectomy first and at a later stage remove or eradicate the source of infection.

MILLER, Chicago.

REPORT FROM THE SECTION OF ORTHOPEDICS. Proc. Roy. Soc. Med. **18**:25 (June) 1925.

R. C. Elmslie reported a case of scoliosis with paraplegia. The patient was a boy, aged 12. Scoliosis was first noticed by the school doctor. Five months later the patient had influenza and from that time was never well. Scoliosis extended from the seventh cervical to the fourth dorsal vertebrae. There was complete motor paralysis of abdominal muscles and whole of lower limbs with spasm, hips and knees flexed, kneejerks and bilateral ankle clonus were present; sensation was normal. Iodized oil injected into cisterna magna was seen by the roentgen ray to have passed down as far as the body of the first dorsal vertebra. As far as the author was able to trace in the literature, no case has been recorded of paraplegia resulting from a scoliotic curve and he feels sure in this case that paraplegia was definitely due to the scoliosis.

H. A. T. Fairbank, President, reported a case of unilateral imperfect formation of the hip joint; subluxation with spontaneous recovery in a girl, aged 2 years.

E. Laming Evans reported a case of osteogenesis imperfecta in a girl, aged 2 years.

WILLIAMSON, New Orleans.

DIFFERENTIAL DIAGNOSIS IN APPENDICITIS IN CHILDREN. WOLF, München. med. Wchnschr. **72**:304, 1925.

The author observed that in questionable appendicitis the psoas symptom is of great help. He observed the child walking; usually the first steps were quite normal, then there was a noticeable limp, the child protecting the right leg. The infant also favors the right leg when kicking.

GROB, Rochester, Minn.

Miscellaneous

A Radiometric Investigation of the Germicidal Action of Ultraviolet Radiation. W. W. Coblentz and H. R. Fulton, Am. J. Electroth. & Radiol. **43**:251 (July) 1925.

This is an abstract of a scientific study by the U. S. Bureau of Standards and the Bureau of Plant Industry. It was shown that ultraviolet radiation possessed germicidal action throughout the spectral range, but that the shortest rays had the most violent lethal action.

[Arch. Derm.]

The Therapeutics of Light. W. E. Dixon, Am. J. Electroth. & Radiol. **43**:363 (Oct.) 1925.

The eruptions of hydroavacciniforme and summer prurigo are attributed to the action of light rays on a substance such as hematoporphyrin, which has the property of fluorescence. The fluorescence of the skin surface in these diseases and in lupus erythematosus and some eczemas is regarded as a protective phenomenon. The presence of cholesterol, which becomes yellow after prolonged exposure to ultraviolet rays, is thought to be a factor in skin pigmentation, and the antirachitic effect of these rays is attributed to the activation of the cholesterol in the superficial layer of the skin.

[Arch. Derm.]

Light and Some of Its Spectral Components in Therapeutics. F. C. Balderrey, Am. J. Electroth. & Radiol. **43**:439 (Dec.) 1925.

The therapeutic action of various forms of light energy is attributed to biologic rather than to germicidal action. Cutaneous tuberculosis was found more responsive to the carbon arc light than to ultraviolet light. The healing of indolent ulcers by ultraviolet light is attributed to irritant action similar to that resulting from the use of chemicals.

[Arch. Derm.]

Symptoms from Teething. A. B. Marfan, Nourrisson **13**:285 (Sept.) 1925.

Although Marfan agrees with the modern school that teething is a perfectly normal physiologic phenomenon in the well developed, healthy infant, still he feels that in other infants less favored in heredity and development, local and general disturbances sometimes occur and that the modern pediatrician should not be too prejudiced to overlook this possibility after he has been careful to rule out all other causes. When the gums are swollen and inflamed, the infant gives evidence by putting its fingers and playthings into the mouth and has an excessive outpouring of saliva. The general symptoms are irritability, crying, insomnia and stationary or declining weight curve. These symptoms are most likely to occur in the artificially fed, especially if they have rickets. Nervous instability due to a tainted heredity is also mentioned as a factor.

When there is an actual infection of the tooth sac, with a collection of seropurulent secretion under the swollen gum, a marked febrile reaction with nervous symptoms may be present. In these cases it is advisable to incise the gum with a crucial incision, and evacuate the contents of the follicular sac. After this, the contingent symptoms promptly subside. The infection may spread and give rise to an ulceration stomatitis, with its usual symptoms.

McClelland, Cleveland.

THE SIGNIFICANCE OF THE TRYPANOCIDAL SERUM SUBSTANCES IN THE HEALING OF CHILDREN'S DISEASES. B. LEICHTENTRITT, Klin. Wchnschr. **4**:1899, 1925.

The serum of a healthy child, injected into a mouse, stimulates its reticulo-endothelial system to antibody production so that it is capable of combating a trypanosome infection. If the reticulo-endothelial system is blocked, the protection is not realized. The serum of children improperly nourished or otherwise unwell, confers little or no protection.

ARTHUR P. LOCKE.

Society Transactions

CHICAGO PEDIATRIC SOCIETY

Regular Meeting, Dec. 15, 1925

GEORGE E. BAXTER, M.D., *President, in the Chair*

FEEDING WITH COW'S MILK. Presented by DR. JOSEPH BRENNEMANN, Chicago.

The younger man who today writes a feeding formula of "so much milk, so much water, and so much sugar, boil two to three minutes," may not realize that that simple formula is the outcome of a long, often painful, and at times acrimonious evolution which has taken place largely in the last thirty years.

It is agreed by all that milk must be the basis of every attempt to feed a young mammal of any kind. The milk of each mammal is, however, specific for its own species only and apparently nonspecific for all other mammals. To overcome this nonspecificity is the problem of artificial infant feeding.

The simplest and most persistent modification has been dilution. Just why it is done is not yet known. It simply works better. If milk is boiled for a long time, acidified, or alkalinized, it can be given straight very early.

The earliest scientific attempts were directed to making a one formula milk that would act like mother's milk. Meig's, Pepper, Rotch, Biedert, Friedenthal, Schloss, and recently Gersternberger have all attempted it, with increasing success.

Each of the food elements, the casein, the fat, the sugar and the salts, and latterly the lactalbumin, have all been blamed for the failure of cow's milk to act like mother's milk. Each in turn has been wholly exonerated, in itself, and some of them have been extolled as having special therapeutic virtues, especially the casein and lactalbumin.

Formerly, lime water and sodium citrate were used very extensively. At present, acids are in vogue.

From Biedert's time on, pediatricians were afraid of overfeeding. The food elements used to be figured in percentages and later the total food in calories, so as not to overfeed. Now pediatricians are told that underfeeding is one of the greatest causes of nutritional disturbances.

All the milk was once sterilized; then it was given raw; now it is boiled, practically, both for bacteriologic and physiologic reasons. It was once thought that young babies could not digest starch; then it was dextrinized. Now it is given by the tablespoonful to babies with pyloric stenosis, aged 3 weeks.

It used to be considered a sacred duty to examine and count stools. For a time they were examined microscopically, at some centers. Latterly, fecal leukocyte counts have been advocated as a measure of pathology. In many places stools are no longer examined at all.

Much more could be said along the same lines, the sugars for instance. All this is not being said in a spirit of levity. It was, and is, all very real. It shows how difficult and complex the problem was, and how grateful the younger physicians ought to be that it has been simplified. These things need emphasis, so that the younger physicians will understand why the older ones do not always share the enthusiasm over the younger physicians' latest panacea. So many panaceas have been outlived.

In general, feeding is now very simple. Nearly all babies can be fed on simple diluted milk plus sugar. Those who cannot will almost invariably thrive on that greatest of all therapeutic foods, protein milk, if it is used properly, and the technic is simple.

Condensed and Dried Milks.—These might be considered together, were it not that one hates to insult the latter by associating it with the former.

Condensed milk is generally considered the most dangerous food to recommend for a baby. Before the advent of protein milk, it had a certain field of therapeutic usefulness. It is apparently the surest and most extensive producer of rickets known. It is further peculiarly dangerous and objectionable because it is so easily digested, so fattening and therefore continued indefinitely, and also because of the pernicious activity of at least one company in prescribing for and advising mothers from the "home office," and is now spreading under a scientific guise a pseudoscientific propaganda among physicians.

Powdered milk, such as Dryco and Klim, is not in the same category. I am inclined to think that its use will be extended in the future. It is especially useful in traveling; when good milk is not procurable, and in certain types of indigestion. It is a safe food to use for a long time.

FACTORS OTHER THAN FOOD WHICH ENTER INTO THE PROBLEM OF THE ARTIFICIALLY FED BABY. Presented by DR. C. G. GRULEE.

The difference was mentioned between the ways that infants were treated in the days of the old milk commission, when milk was given from milk stations and at the present time, when these children were given individual care in the home and individual formulas. It seemed to him that the reason for this was more in the way that the children were treated than what they were fed. He called attention to the environmental factors: cleanliness, fresh air, humidity, clothing and bedding, and how much had been accomplished in reducing gastrointestinal disturbances by careful attention to these factors. He then called attention to the psychologic side of infant feeding—how much the baby was influenced in its psychology by its attendants, and how much this had to do with success in infant feeding.

He concluded his remarks with the following: "I would sum up, then, by saying that, not only during the past years have we learned some of the failures of infant feeding from the standpoint of food, but we have learned many of the failures from the standpoint of environment of the child, and, to my way of thinking, emphasis on and attention to the environment of the child and hygienic conditions are just as important as emphasis on the food which is to be put into that child's mouth."

TECHNIC OF ADMINISTRATION OF PROTEIN MILK IN INFANT FEEDING. Presented by DR. ISAAC A. ABT.

Dr. Abt believed that one should add at least 3 per cent carbohydrate at the very onset, or 5 per cent carbohydrate might be used at the start, and give from 180 to 200 cc. of the protein milk per kilogram of body weight.

In older children, who are underweight and need considerable food, as a rule, one should not exceed 1,000 cc. In treating dystrophic children, if the weight remains stationary, the sugar may be increased to 7 or 10 per cent. If the baby is 6 or more months old, other food may be added to the protein milk mixture.

Corn-starch or finely ground flour may be added to the milk, or be given as a separate feeding. Milk sugar should be avoided because of its tendency toward the production of fermentation.

When the patient does well with this food, the stools should improve rapidly and soon become soap-like. This might happen within three days or as early as twenty-four hours after the feeding has been started. The actual improvement or gain in weight does not occur until the carbohydrate is added, and, if the carbohydrate is added at first, the improvement is rapid.

The so-called reparation depends on the severity of the attack and the age of the patient, although, if protein milk is given, the reparation period is short.

If the infant does not improve at once with this food, and the stools do not become soap-like, the protein milk should be continued and not decreased in amount. To decrease it is a technical error. If the quantity of protein milk is diminished below the needs of the infant, inanition symptoms occur. If the carbohydrate is diminished below the baby's demands the condition of the infant is influenced.

If from 2 to 5 per cent of carbohydrate is insufficient, from 6 to 7 per cent may be added. Sometimes, even with good stools, the weight diminishes and the temperature remains subnormal. This may be remedied by the addition of carbohydrates.

The continuation of bad stools should not be a contraindication for the use of protein milk and carbohydrates. Even in spite of unfavorable appearance of the stools, food should be given and the carbohydrates increased until the baby gains in weight. In dyspepsia, one should begin with 10 ounces of protein milk and 5 per cent of carbohydrate after six to twelve hours of a tea diet, and this should be increased until the baby is receiving from 6 to 7 ounces per kilogram of body weight, and carbohydrate should be increased to 6 or 7 or even 10 per cent.

Finklestein says that, if in spite of this food no gain in weight occurs, sugar should be increased even to 20 per cent.

DISCUSSION

DR. I. A. ABT: The doctor's personality counts for quite as much as the peculiarities of the mother. He should be able to gain her confidence and to secure her cooperation. The nurse is a very important factor in these modern days of child rearing. Everyone knows that nurses are variable factors. Some are cooperative, some are refractory, and some occasionally are impossible. A good nurse who is willing to cooperate, who enjoys her work, and has a conscientious regard for the baby is an important and necessary person. A nurse who understands her infant, who feeds him regularly, handles him quietly and calmly, who shows common sense in the general management of her charge does more very often than the infant's mother, because the latter has no experience and she is usually doing other things than those which pertain to the care of her baby.

DR. JULIUS H. HESS: The question of the use of proprietary foods for the feeding of infants being up for discussion this evening, I thought that some of the correspondence in my files and a discussion of advertisements to the laity by manufacturers might be of some interest to the members.

I wish first to present to you an advertisement now being used by a well known dry milk company, that, I think we can say without reservation, owes

much of the popularity accorded its product to the medical profession: ". . . is superior as a nutrient agent to raw milk, modified milk, or artificial combinations of milk with starch, sugar or fat, not only for the feeding of infants but also for the nourishment of acutely ill, convalescent or invalid patients."

On receiving a copy of the foregoing advertisement for insertion in *The Trained Nurse and Hospital Review*, the managing editor of that journal raised the question with the manufacturers as to the basis for these claims and received the following letter:

"On the writer's return from abroad, he was handed your letter of January 17. Referring to same, we should first like to ask you why you wish us to modify a truthful statement which is backed up by clinical and scientific data? It is part of our business to educate the public, and the doctor in particular, who has no time to study the question that dry milk, and especially (name of brand), is superior to raw milk or to modified milk. We can submit enough data to anyone interested to prove this. If your magazine does not wish to print the truth, kindly discontinue our advertising. If you can point out any statements in our advertisements that are not absolutely true, we ask you to do so.

"Yours very truly,

"(Signed) V. P. and Mgr."

Without discussing it further, I ask members of this society to draw their own conclusions as to the merits of the foods discussed and as to the question of ethics involved.

The next exhibit is a full page advertisement of Karo, taken from *The Boston Post*, a daily newspaper, of Dec. 5, 1924, with the heading: "How the Greatest Nourishment for the Least Money Was Achieved for Thousands of Children by the Near East Relief. A Lesson for American Mothers Taught by Orphans of the Near East."

Photographs bearing the following legend are printed in this advertisement: "Two examples of what the Near East Relief has achieved in transforming half-starved orphans into robust, healthy children. Please read the message above."

The following are extracts from advertising material appearing in *Hygeia*:

"The fact that thousands of physicians are feeding S. M. A. with uniformly successful results, to normal full-term infants from a few days to one year of age or more, *without any qualitative change, whatsoever*, is convincing proof of the resemblance of S. M. A. to breast milk in all important respects.

"Thousands of physicians have found S. M. A. helpful in their problems of feeding infants deprived of breast milk, *since most infants do exceedingly well on it.*"

Another advertisement from *Hygeia* is as follows: "Horlick's—The Original Malted Milk. A safe, reliable infant food. Endorsed and prescribed by the medical profession over one-third of a century. Send for infant feeding literature."

Dr. Brennemann has spoken of condensed milk. I think we will all agree that the results in the feeding of normal infants by the Infant Welfare Society of Chicago, and the Infant Welfare Stations of the Health Department of the city of Chicago, have, on the whole, been very successful. Both of these organizations have a rule that only cow's milk, water, or cereal water, sugar, cod liver oil, and fruit juices are to be used in feedings prescribed at their various stations.

Manufacturers of proprietary foods are not looking for the exceptional baby. It alone is not a profitable customer. They are concerned with the feeding of the well baby. I wish again to stress the fact that it is our province to teach the young physician how to feed the young infants properly, and to keep them well. This can be accomplished by prescribing diets over which he has complete control.

DR. L. W. SAUER: The more I learn about the feeding of infants, the more convinced I become that it is based on the following ironclad principles:

1. The great majority of infants, whose food tolerance has not been overstepped, will respond in a physiologic way to breast milk, protein milk or cow's milk mixtures, provided the food is proper in quality and quantity for the age and weight of the child.

2. Breast milk agrees with more infants than does any artificial food.

3. Protein milk, properly proportioned, is the safest substitute for breast milk in the young infant.

4. Cow's milk, properly diluted and enriched with carbohydrate, is usually well borne by infants over 10 pounds (4.5 Kg.) in weight.

5. Thriving, artificially-fed infants seldom need changes of formula oftener than once a month.

6. Strengthening a formula too soon not infrequently causes a reduction in the infant's digestive capacity and tolerance.

7. Infants who fail to thrive on a theoretically correct formula deserve painstaking study and frequent supervision.

8. Clinical analysis often reveals an intolerance or reduced tolerance for fat, sugar, protein or whey-salts, or the presence of a parenteral infection.

9. Temporary or partial use of breast milk for a week or more often improves the tolerance for the food element in question.

10. All artificially fed infants need cod liver oil, orange juice, fresh air and sunlight.

DR. W. H. O. HOFFMANN: Since for years I have been teaching physicians who specialize in infant welfare, I know something of their persistent resistance to simplicity. When it comes to sugar, it is dextrimaltose or it is Karo syrup, depending on which salesman has seen them last. I believe Dr. Brennemann's statements are the best I have ever heard. We have the best infant's food today in cow's milk and sugar.

DR. C. G. GRULEE: There is only one thing I would like to add. It seems to me the most serious thing we have to deal with today is the question of impressing on the medical profession that infant feeding is a simple thing. Ninety-five per cent of the cases can be handled with the ordinary milk mixtures, water and sugar. If we can once impress that fact on the medical profession, we do not have to pay any attention to all these advertisements that Dr. Hess has taken the trouble to present to us. I feel it is most important, from the standpoint of infant feeding, to get the doctor to realize that this feeding is comparatively simple. We are still living on the old psychology of algebraic equations. Dr. Brennemann, Dr. Abt, Dr. Hess and myself, and probably several others, remember the days when we had to figure out all the formulas to the *n*th decimal point. Then some one was kind enough to show that we could not get within 0.5 per cent of the formula. We must teach the general profession that infant feeding is a simple matter.

NEW ENGLAND PEDIATRIC SOCIETY

Boston, Mass., Jan. 8, 1926

JOHN LOVETT MORSE, M.D., *in the Chair*

CHRONIC FATIGUE IN THE SCHOOL CHILD—A PSYCHOPHYSIOLOGIC STUDY. Presented by DR. MAX SEHAM, Minneapolis, Minn.

Dr. Seham emphasized the fact that fatigue is intimately related to every-day life, and that the child is highly susceptible to chronic fatigue as a result of which he lacks adequate preparation for his school work; his inhibitory and coordinating mechanism are relatively poorly developed, and his emotional reactions are easily rendered abnormal.

He made a very extended and painstaking investigation of a large number of school children, and put them through numerous tests in order to assume the quantity and quality of fatigue. He also had questionnaires filled out from which further data were obtained and included. As a result of this investigation, his chronic fatigue may be defined as a psychophysiologic syndrome of more than three months duration, the state of subefficiency manifesting itself in four ways: (1) Feelings of fatigue; (2) actual decrease in the individual's average mental achievement; (3) decrease in the individual's average physical strength and endurance, and (4) emotional unbalance.

There was no way of measuring the degree or amount of fatigue to objective tests. Dr. Seham feels that the diagnosis of chronic fatigue is justifiable when there are feelings of fatigue, and also one of the three before-mentioned factors. He suggests a program of rational habits which he believes applicable to the individual child attending public schools.

DISCUSSION

DR. F. B. TALBOT: The subject that Dr. Seham has brought up is the commonest diagnosis that we have in private practice. In many instances it is the hardest condition with which we have to deal. The daily nap is omitted far too early.

There is no question in my mind that improper bodily mechanics is one of the most important elements in chronic fatigue, and that although it can be corrected by a summer vacation or by rest, it is not always possible to send a child off on a vacation; it is possible to overcome the poor body mechanics by corrective exercises.

DR. KENNETH D. BLACKFAN: I was much interested in hearing what Dr. Seham had to say about the important question of fatigue. He has added, I think, something else for us to do in this peculiar type of child. We have been educated to correct the physical defects and the diet of the child, and now Dr. Seham has presented to us the very interesting problem of regulating the life activities of the child. He has done it in a careful way and his talk should be of great help to us.

DR. CHURCHILL: Dr. Seham's interesting work is going to have a more widespread and far-reaching effect than most of us realize.

I attended a meeting of the Juvenile Court in the West last year. There were a good many cases brought up before the judge, and a considerable number of them would have fitted into Dr. Seham's abnormal class. I cannot but feel that this sort of work is striking right at the roots of one of

the most serious problems in this country. I believe that the study of such children as these, with the application of Dr. Seham's methods, is going to do a great deal to prevent great numbers of children coming to the Juvenile Court.

DR. HILL: Dr. Seham's paper has struck a very popular note in our profession.

I think the question of sleep is one of the most important points in this subject, and that the daily nap is essential for these young children; yet you find very few children over 4 years of age taking a nap. They grow out of the habit.

This leads to another point to which I am greatly opposed, and that is two sessions of school. I think it is one of the worst phases of school life with which we have to deal.

DR. SEHAM (closing): As I go on with this study, I shall probably change some of the titles of my subdivisions. I feel quite sure that there is something in fatigue which we can help to avoid, and that we ought to try to help these abnormal children to live a life as nearly like that of a normal child as possible.

Book Reviews

Scoliosis. By Samuel Kleinberg, M.D. Price, $6. Pp. 211, with 140 illustrations. New York: Paul B. Hoeber.

The contents of this book have been divided into chapters dealing with the anatomy, physiology, pathology, etiology, examination, clinical records, symptoms, prophylaxis and treatment by gymnastic exercises, forcible correction and operative measures with the prognosis.

Long theoretic discussions have been omitted, leaving the text composed of practical and useful features. Although it was written for orthopedic surgeons, the family physician should comprehend the essentials of this deformity, and would be in a better position to advise the patient after reading this book.

The author has honestly and without prejudice presented the prognosis and course of this condition, with the various forms of treatment. It is profusely illustrated with good photographs representing the various phases of the subject.

The publisher's work has been well done in that the paper is good, the type is large and distinct, the margins are wide and the illustrations are very good. All these features make this a book which is easily read.

Health Through Prevention and Control of Diseases. By Thomas D. Wood, M.D., and Hugh Grant Rowell, M.D. Pp. 119. Chicago: World Book Company, 1925.

This little book of 119 pages gives a comprehensive idea of what can be accomplished by making the school a health center. Definite advice is given as to how to meet the various emergencies, and definite rules are laid down for both teachers and parents as to when children should be excluded from school and when they should be allowed to return. A complete, concise chapter regarding contagious diseases is given. The book can be recommended for parents and teachers as well as for school physicians and nurses.

THE AMERICAN JOURNAL OF DISEASES OF CHILDREN is published by the American Medical Association as a means for the advancement of knowledge of the diseases of children and for the publication of scientific investigation in this field.

Manuscripts for publication, books for review, and correspondence relating to the editorial management should be sent to Dr. Clifford G. Grulee, 104 South Michigan Avenue, Chicago, or to any other member of the Editorial Board. Communications regarding subscriptions, reprints, etc., should be addressed, AMERICAN JOURNAL OF DISEASES OF CHILDREN, American Medical Association, 535 North Dearborn Street, Chicago.

Articles are accepted for publication on condition that they are contributed solely to the AMERICAN JOURNAL OF DISEASES OF CHILDREN. Manuscripts must be typewritten, preferably double spaced, and the original copy should be submitted. Zinc etchings and halftones of illustrations will be supplied by the Association when the original illustrations warrant.

Footnotes and bibliographies should conform to the style of the Quarterly Cumulative Index, published by the American Medical Association. This requires, in order given: name of author, title of article, name of periodical, with volume, page, month—day of month if weekly—and year. A complete list of abbreviations for standard periodicals, together with a full discussion of the style of the A. M. A. publications, appears in The Art and Practice of Medical Writing, a comprehensive book on the preparation of medical manuscripts, published by the American Medical Association. Price, $1.50.

Matter appearing in the AMERICAN JOURNAL OF DISEASES OF CHILDREN is covered by copyright; but, as a rule, no objection will be made to its reproduction in reputable medical journals, if proper credit is given. However, the reproduction for commercial purposes of articles appearing in the AMERICAN JOURNAL OF DISEASES OF CHILDREN or in any one of the other publications issued by the American Medical Association will not be permitted.

Authors will receive one hundred reprints free; additional reprints may be obtained at cost.

The AMERICAN JOURNAL OF DISEASES OF CHILDREN is published monthly. Annual subscription price (two volumes): Domestic, $4.00; Canadian, $4.30; foreign, $4.50, including postage. Single copies, 50 cents, postpaid.

Checks, etc., should be made payable to the AMERICAN MEDICAL ASSOCIATION.

OTHER PERIODICAL PUBLICATIONS
of the American Medical Association

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION—Weekly. Covers all the medical sciences and matters of general medical interest. Illustrated. Annual subscription price (two volumes): Domestic, $5.00; Canadian, $6.50; foreign, $7.50. Single copies, 20 cents.

ARCHIVES OF INTERNAL MEDICINE—Monthly. Devoted to the publication of advanced, original clinical and laboratory investigations in internal medicine. Illustrated. Annual subscription price (two volumes): Domestic, $5.00; Canadian, $5.40; foreign, $5.75. Single copies, 75 cents.

ARCHIVES OF NEUROLOGY AND PSYCHIATRY—Monthly. A medium for the presentation of original articles on nervous and mental diseases, with abstracts from foreign and domestic literature, book reviews, society transactions, etc. Illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75. Single copies, 85 cents.

ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY—Monthly. Devoted to advancing the knowledge of and progress in cutaneous diseases and syphilis. Publishes original contributions and full abstracts of the literature on these two subjects, transactions of the important dermatological societies, book reviews, etc. Illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75. Single copies, 85 cents.

ARCHIVES OF SURGERY—Monthly. Devoted largely to the investigative and clinical phases of surgery, with monthly reviews on orthopedic and urologic surgery. Well illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75. Single copies, 85 cents.

ARCHIVES OF OTOLARYNGOLOGY—Monthly. A medium for the presentation of original articles on diseases of the ear, nose and throat, with abstracts from foreign and domestic literature, book reviews, the transactions of special societies, etc. Illustrated. Annual subscription price (two volumes): Domestic, $6.00; Canadian, $6.40; foreign, $6.75. Single copies, 75 cents.

ARCHIVES OF PATHOLOGY AND LABORATORY MEDICINE—Monthly. A periodical devoted to the publication of original contributions in the field of pathology, with abstracts from foreign and domestic literature, book reviews, the transactions of special societies, etc. Illustrated. Annual subscription price (two volumes): Domestic, $6.00; Canadian, $6.40; foreign, $6.75. Single copies, 75 cents.

QUARTERLY CUMULATIVE INDEX TO CURRENT MEDICAL LITERATURE—Quarterly. A complete subject and author index to the worth-while current medical literature of the world. Issued four times a year. Second and fourth volumes bound for permanent reference. Subscription price, calendar year: Domestic, $8.00; Canadian, $8.50; foreign, $8.75.

AMERICAN MEDICAL ASSOCIATION

535 North Dearborn St. **CHICAGO**

CONTENTS

PAGE

THE PREVENTION OF RICKETS: THE INFLUENCE OF THE ROUTINE ADMINISTRATION OF COD LIVER OIL IN THE PREVENTION OF RICKETS IN INFANTS. MAY G. WILSON, M.D., NEW YORK.. 603

DUODENAL ULCER IN MELENA NEONATORUM: ETIOLOGY AND HEALING PROCESS. ROGER L. J. KENNEDY, M.D., ROCHESTER, MINN. 631

OSTEOMALACIA IN CHILDREN: A STUDY OF THE MINERAL METABOLISM. HUGH L. DWYER, M.D., AND ORREN S. ECKELBERRY, A.B., KANSAS CITY, MO. 639

CHYLOTHORAX IN THE NEW-BORN INFANT: REPORT OF A CASE. CHESTER A. STEWART, M.D., AND H. P. LINNER, M.D., MINNEAPOLIS 654

RECURRENT VOMITING. HUGH JOSEPHS, M.D., BALTIMORE..... 657

INFLUENCE OF ACIDIFIED MILK ON DUODENAL FUNCTION IN INFANTS. LLOYD ARNOLD, M.D., CHICAGO..... 668

GOITER IN CHILDREN IN NEW YORK CITY: THYROID SURVEY OF 11,084 SCHOOL GIRLS AND 783 SCHOOL BOYS. FRANCES COHEN, M.D., NEW YORK..... 676

THE KIDNEY: A FILTER FOR BACTERIA. VI. THE EFFECT OF URETERAL OBSTRUCTION ON THE EXCRETION OF BACTERIA. HENRY F. HELMHOLZ, M.D., AND RUTH S. FIELD, B.A., ROCHESTER, MINN..... 693

PROGRESS IN PEDIATRICS:

FLATFOOT IN INFANTS AND IN CHILDREN. PHILIP LEWIN, M.D., CHICAGO 704

CORRESPONDENCE:

ACIDIFIED MILK. HAROLD K. FABER, M.D., SAN FRANCISCO.. 719

NEWS AND COMMENT:

DEATHS OF PEDIATRICIANS ABROAD..... 719

BREAST FEEDING DEMONSTRATION..... 719

ABSTRACTS FROM CURRENT LITERATURE..... 720

SOCIETY TRANSACTIONS:

CHICAGO PEDIATRIC SOCIETY..... 755

NEW ENGLAND PEDIATRIC SOCIETY..... 760

BOOK REVIEWS..... 762